Allergy Abstracts

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Allergy Abstracts

Asthma and Hay Fever

Ethylene Disulfonate in Bronchial Asthma. A Preliminary Report. Kurland, L. T., and Bubert, H. M.: Bull. School, Med. Univ. Maryland **30**: 46, 1945.

The administration of ethylene disulfonate for the treatment of allergic diseases was first suggested in 1940 by Evan, Bodman, and Maisin. They offered a fantastic theoretical explanation of the basic process of allergy. They stated that "Shock whether traumatic, infective or emotional, interferes with the normal action of certain dehydrogenetic catalysts, thus preventing the normal degradation of carbohydrates by means of which oxygen is freed and energy released." They contended that the shock inactivated one of the series of coenzymes normally present and felt if this could be supplied in minute amounts it would re-establish the process. Ethylene disulfonate was thought to be the substance which might replace that part of the dehydrogenase coenzyme system which was absent or paralyzed by shock. The authors claimed that ethylene disulfonate inhibited anaphylactic shock in guinea pigs, and they also reported an exceptionally high percentage of successful results following the clinical use of this substance. Several other workers failed to confirm these experimental or clinical results.

In the present study, twelve patients suffering from chronic bronchial asthma of either the intrinsic or extrinsic type were treated with ethylene disulfonate according to the procedure suggested by its originators. The average duration of the condition was fifteen years, the shortest being two and the longest thirty years. The average period of observation during ethylene disulfonate therapy was seventeen weeks. Five patients (41 per cent) failed to obtain any relief; three (25 per cent) were slightly improved; and two (16.5 per cent) were definitely improved. There were no cures. The results indicated that the claims which had been made for ethylene disulfonate were excessive, and that this preparation had little if any therapeutic value. A.

The Association of Periarteritis Nodosa, Bronchial Asthma, and Hypereosinophilia. Wilson, K. S., and Alexander, H. L.: J. Lab. & Clin. Med. **30**: 361, 1945.

A review of three hundred consecutive reported cases of periarteritis nodosa, proved by tissue section, has been made, starting in 1914. Over half of the present series occurred during the years 1940 to 1943, inclusive. A total of fifty-four patients had bronchial asthma, an incidence of 18 per cent. The average age of onset of the asthmatic paroxysms in this series was later than usual, less than 15 per cent starting in the first two decades. It was unusual for an extrinsic cause of the asthma to be found. The asthma was severe in most cases. Blood counts were done on forty-seven asthmatic patients. Forty-four had eosinophilia of from 11 to 84 per cent with an average of 53.5 per cent. In sharp contrast, 151 periarteritis patients without asthma had an average blood eosinophile count of 2.5 per cent, and only nine of these patients had hypereosinophilia. The coincidence of a high blood eosinophilia and severe bronchial asthma in an adult should provoke suspicion of an underlying periarteritis nodosa. E. Kailin.

Fatal Bronchial Asthma Showing the Asthmatic Reaction in An Ovarian Teratoma. Thomson, J. G.: J. Path. & Bact. **57**: 213, 1945.

A 47-year-old woman who had had bronchial asthma "for years" had a typical asthmatic attack relieved by adrenalin at 11:00 P.M. on the day of hospital admission. At 1:00 A.M. she was given ¼ grain of morphine because of restlessness. At 8:30 A. M. she was cyanotic and in shock. She died a half hour later. At autopsy an ovarian teratoma containing respiratory tissue was found. This dermoid respiratory tissue showed the same esoinophilic infiltration, Charcot-Leyden crystals, and thickened basement membrane which were found in the lungs. No other part of the teratoma or other organ of the patient was similarly affected.

The histologic findings in the lungs were described in detail and presented a typical picture of bronchial asthma. E. Kailin.

Simultaneous Registration of Intrathoracic, Right Intracardiac and Systemic Pressure in Man. Bloomfield, R. A.: Proc. Soc. Exper. Biol. & Med. **60**: 75, 1945.

In the investigation in human beings of the circulation through the right side of the heart under conditions of unusual respiratory effort or in the presence of abnormalities of the pulmonary circulation, a simultaneous recording of right intracardiac pressure and intrathoracic pressure is essential. A technique for measuring right intracardiac pressures in human subjects was previously described. In the present communication a method for recording intrathoracic pressure is outlined. The apparatus consists of a specially designed recording manometer with a mirror and a pleural catheter. As soon as the catheter has been inserted into the pleural space it is attached to the recording manometer, and the valve is opened. The pressure is recorded optically by means of a light beam. Illustrations of several tracings are included in the report. A.

Nebulized Penicillin: Preliminary Report of Its Role, in the Management of Surgical Bronchiectasis. Olsen, A. M.: Proc. Staff Meet., Mayo Clin. **20**: 184, 1945.

Seven patients with bronchiectasis treated preoperatively with aerosolization of penicillin were benefited. The quantity of sputum raised in the preoperative period was sharply reduced in several cases. The risk of operation was definitely reduced. Most of the patients had less trouble with secretions after operation. Prolonged daily treatment seemed to be desirable. With alternating ten-minute periods of nebulization and rest, 5 c.c. of the solution could be nebulized every hour. The daily period of treatment lasted ten hours. It has been demonstrated that the bactericidal effect of penicillin requires a constant exposure of the organisms to the drug for a period of four to six hours. In nonsurgical bronchiectasis the results obtained with nebulized penicillin have been encouraging, but the observation period is too short to justify drawing final conclusions. The treatment is primarily aimed at the bronchial infection which is a complication of bronchiectasis. H.

A New Method of Aerosolization of Penicillin, Sulfonamides and Other Medications for Inhalation Therapy. Prigal, S. J., and Speer, F. D.: Bull. New York M. Coll., Flower & 5th Ave. Hosp. **8**: 21, 1945.

The authors have successfully employed for aerosal formation a combined steam generator and aerosolizer, which they claim is simple and economical.

Five to ten minutes after the current is turned on, steam begins to emerge from the spout. The spout is specially designed to connect with a tube which extends into the container holding the medication. The vacuum created in the tube allows the medication to be drawn up and expelled from the nozzle in a fine mist mixed with steam. Using this therapeutic procedure, effective and prolonged therapeutic blood levels of sulfadiazine and penicillin were obtained. Clinical studies with aminophylline indicated that this medication in aerosal form could furnish relief to many asthmatic patients. H.

Asthmatic Atelectasis Simulating Pneumonia. Cole, D. B., Nalls, W. L., and Buis, L. J.: Virginia M. Monthly **71**: 505, 1944.

Radiographic studies of asthmatic patients who suddenly experience chest pain accompanied by increased respiratory and pulse rates and a slight rise in temperature usually show an area of atelectasis. Four such cases are presented. Two of these patients manifested symptoms simulating pneumonia. Coughing should be encouraged to remove the obstruction. Bronchoscopic aspiration is advised if simple measures fail. Chemotherapy has been found ineffective. Carbon dioxide inhalations may be helpful. Oxygen should be used cautiously. H.

Eosinophilic Lung (Tropical Eosinophilia). Hodes, P. J., and Wood, F. C.: Am. J. M. Sc. **210**: 288, 1945.

This is a disease which may be found in troops returning from the Orient. The etiological role of the cheese mite, *Tyroglyphus,* and related parasites has not been established although these have been reported in sputa of patients with eosinophilic lungs. Season, race, age, diet, and social status are not etiological factors. Common symptoms are fever, cough, wheezing, and expiratory dyspnea, usually worse at night. The usual duration is several weeks, but untreated cases may develop chronic bronchopulmonary symptoms. Mild cases may only present roentgenographic findings and a blood eosinophilia. The total white blood count is usually over 20,000 and may reach 80,000. Eosinophiles may constitute 92 per cent of the total white count. Two cases are presented. Neoarsphenamine given every fourth day usually clears the condition by the third injection. Tropical eosinophilia is probably an entity distinct from Loeffler's syndrome. E. Kailin.

Some Experience With Small Dosage Dust and Pollen Therapy. Hansel, F. K.: South. M. J. **38**: 608, 1945.

Satisfactory results were obtained by treating dust-sensitive patients with small doses of stock house dust extract. The stock extract was prepared from the following ingredients: vacuum cleaner sweepings, old mattress stuffing, automobile upholstery vacuum collections, kapok, feathers, jute, and ozite. Animal dander, silk, *Pyrethrum,* tobacco, or specific environmental dusts were added separately when indicated. In some cases an extract of old feed mill dust, consisting almost entirely of molds, was used either alone or added to the stock dust extract. Skin testing was performed with a 1:10 dilution of stock dust. This was the maximum concentration used for skin testing and yielded some irritating reactions. The severity of clinical symptoms, however, was considered to be a more reliable indication of relative sensitivity. The optimum dosage of dust extract varied from 1:10,000,000 to the 1:10,000 dilutions in adults and from 1:10,000,000 to 1:1,000,000 in children. Doses were increased by 0.05 c.c. until a maximum tolerance was reached. When satisfactory relief

was attained, no further increase in dosage was attempted. The time intervals between injections were gradually increased from once a week to ten, fourteen, or twenty-one days. In some cases treatment was discontinued after relief was obtained and many patients remained free of symptoms for long periods of time.

Many cases of summer hay fever and asthma negative to pollen skin tests were treated satisfactorily with small doses of mold extract made from old feed mill dust. Vernal conjunctivitis was also successfully treated with the same extract.

In hay fever patients, the author advocates the use of coseasonal therapy with small doses of pollen intracutaneously. Where possible, coseasonal therapy should be preceded by preseasonal treatment. The initial dosage is determined by the dilution of extract which causes a 15 mm. wheal following intracutaneous injection. If this sized wheal results from a 1:100,000 dilution, treatment is begun with 0.02 c.c. of this dilution and the amount of the injection is increased 0.01 c.c. every two to five days until an optimum dosage is reached. This may be as much as 0.05 c.c. of the 1:10,000 dilution in cases of moderately marked sensitivity. Small doses are also advocated subcutaneously in preseasonal treatment. It is concluded that small doses of pollen yield satisfactory results in the majority of hay fever patients. A.

Dermatology

Dermatitis From Synthetic Resins. Schwartz, L.: J. Invest. Dermat. **6**: 239, 1945.

Synthetic resins frequently called plastics are one of the commonest causes of dermatitis among workers making and using them. Resins are formed either by polymerization or by condensation. In polymerization a number of molecules of the same composition called monomers are united to form a large molecule of the same composition called a polymer. In condensation a number of molecules not necessarily of similar composition are united to form a molecule dissimilar in composition to the components, some compounds being liberated. Catalysts are frequently used to effect polymerization or to cause condensation. Dermatitis is rarely caused by the completely polymerized finished pure resin or by the completely condensed "cured" finished resin. The incompletely condensed resin, the uncombined components or the catalysts may be both primary skin irritants and sensitizers. Resins may be classified as thermo-setting or thermo-plastic according to their reaction to heat. They may also be divided into two types according to their method of formation, i.e., by condensation or by polymerization. Fifteen kinds of resins are enumerated, and the methods of their manufacture are described. The occurrence of dermatitis among workers engaged in the manufacture of resins varies with the type of resin. The incidence of dermatitis also varies at different stages of manufacture for individual resins. Prophylactic measures and precautions which should be taken to avoid dermatitis among workers in the plastic industry are enumerated. A.

Allergic Reactions During the Administration of Penicillin. Lamb, J. H.: Arch. Dermat. & Syph. **52**: 93, 1945.

Similar allergic skin reactions were observed in two patients who received penicillin therapy. In the first case, on the fifth day after 400,000 units of penicillin had been administered for the treatment of actinomycosis, the patient complained of a vesicular eruption on the genitals and on the webs of the fingers. The eruption spread to the crural region and about the scrotum and

was accompanied by severe itching. Within twenty-four hours after the use of penicillin had been discontinued, the eruption was exfoliating and the itching had ceased. The patient had never suffered from dermatophytosis or any other fungus infection. Intracutaneous tests were performed with penicillin, trichophytin, and oidiomycin. A strongly positive reaction was obtained with oidiomycin within forty-eight hours. Negative reactions were obtained with penicillin and trichophytin. Cultures of material from the affected area were negative for fungi. The second patient developed a similar vesicular reaction three hours after penicillin therapy had been instituted for the treatment of syphilis. The drug was continued for four days until the itching became unbearable. The patient gave a previous history of dermatophytosis. An intracutaneous test performed with penicillin resulted in a wheal within thirty minutes. In sixty hours a vesicle was noted at the site of injection. Tests with trichophytin and oidiomycin were negative. Microscopic examination of the vesicles from the crural region revealed fungi and hyphae although cultures were negative for fungi. The author offers several possible explanations for the rashes which occurred in these cases. A.

Cutaneous Detergents. Experience With an Ether Sulfonate Compound. Guild, B. T.: Arch. Dermat. & Syph. **51**: 6, 1945.

The use of soap during the treatment of contact dermatitis may prolong the irritation after the direct cause has been eliminated even if the soap is not the etiological agent. The irritant action of soap is probably due to a combination of the fatty acids and alkali. Of all the detergents used as substitutes for soap, the sulfonate appeared to be the most desirable. Ether sulfonate may be adjusted to a pH 5.5 by the use of a weak nonirritating acid, and suds are produced which also have a pH value of 5.5 which corresponds to the pH of the surface of the skin. The author describes his experiences with a detergent cream (pHisoderm) composed of a sulfonated ether, petrolatum, lactic acid, and wool fat cholesterols. This cream has been used for a period of five years in the allergy and dermatologic clinics of the Massachusetts General Hospital. Three hundred seventy-four patch tests with the detergent cream were included in a series of 8,628 tests with various allergens applied to several hundred patients with normal or abnormal skin. A fraction of 1 per cent of the patients showed vesicular reactions. The same number of reactions were obtained with hydrous wool fat and petrolatum. Seventy-two patients with asthma, hay fever, or allergic dermatitis were patch tested with the detergent cream. All showed negative reactions. Many were retested after two weeks but again showed negative results indicating that the cream has no sensitizing properties. The cream was found to be 40 per cent more effective as a cleanser than is soap. A.

Dermatitis From Benzidine. Baer, R. L.: J.A.M.A. **129**: 442, 1945.

A physician who suffered from recurrent eczematous dermatitis of the hands and face was found to be sensitive to benzidine. Patch tests with this powder were strongly positive. A careful analysis of the history revealed that whenever the patient had performed a benzidine test for blood he had experienced a recurrence of the eruption. F.

Certain Statistical Considerations in Patch Testing. Henderson, C. R., and Riley, E. C.: J. Invest. Dermat. **6**: 227, 1945.

Patch testing procedures may be adapted for the detection and the evaluation of the skin-irritating properties and sensitizing properties of chemical

agents and materials. Certain statistical principles must be applied in order to interpret the results obtained on a test group of subjects in terms of the general population. From a statistical point of view two questions are of importance: (1) If no positive reactions or if a certain number of positive reactions to a patch test are observed in a given test group, what would be the maximum incidence likely to occur, under identical conditions, in a large number of individuals similar to the test group? (2) How large a group must be tested to predict, with a given degree of certainty, that the rate of positive reactions in the general population lies within certain given limits? Statistically, it can be shown that, if no positive reactions occur in one hundred subjects, the rate of positive reactions in the population is not likely to exceed approximately 2.9 per cent, the likelihood being at the 95 per cent level. (The likelihood level of 95 per cent is a measure of the confidence with which it can be asserted that the population rate does not exceed the stated value.) If one reaction is observed in one hundred subjects, the likelihood is 95 per cent that the rate does not exceed 4.5 per cent. Equations are given for arriving at estimations of the maximum rate of positive reactions in the population from which the sample is drawn. The number of positives and the size of the sample are the known factors in the equation. The size of the sample necessary to determine whether the rate of positive reactions in the population does not exceed a given figure can also be estimated by the use of an equation. A.

Otorhinology and Opthalmology

Absorption of Penicillin From the Nose and Alimentary Canal. Chu, W. C., Fiese, M. J., Cutting, W. C., and Collen, M. F.: Proc. Soc. Exper. Biol. & Med. **60**: 159, 1945.

Penicillin was absorbed in rats from ligated sections of the alimentary canal such as the esophagus, stomach, duodenum, ileum, and colon. Assays on blood specimens taken from the heart after thirty minutes indicated that absorption from the alimentary canal was only about one-fifth as great as that from intramuscular injection. Absorptions from the stomach, duodenum, ileum and colon were about equal. Esophageal absorption was much greater. In dogs, penicillin was absorbed from the nose or mouth about one-fourth as well as from intramuscular injection. In man, a study of the intranasal absorption of penicillin indicated that solutions containing 100,000 units per cubic centimeter could be tolerated without significant irritation if they were introduced by spray. When the same solution was dropped into the nose it was irritating. The blood concentration of penicillin following its administration by intranasal spraying was very low and could not be regarded as adequate for the treatment of systemic infections. However, the high local concentration of penicillin in the nose may be of value in the treatment of upper respiratory infections of bacterial origin. C.

Pharmacologic Studies of a New Vasoconstrictor: 2-Napthyl-(l')-Methyl-Imidazoline Hydrochloride (Privine or Naphthazoline). III. An Attempt to Localize the Seat of Action in Terms of Adrenergic and Cholinergic Foci. Yonkman, F. F., Rennick, B., and Schwerma, H. L.: J. Pharmacol. & Exper. Therap. **84**: 194, 1945.

Twenty-four anesthetized cats were prepared so that the salivary flow, the contraction of the nictitating membrane, and the blood pressure could be measured. Privine was administered rectally, orally, intraperitoneally, or directly into the stomach or small intestine. Privine, 0.1 mg. per kilogram of body

weight, elevated the arterial tension. This effect was diminished but not reversed after administration of the sympatholytic drug ethyl yohimbine. Privine in a dose of 1 mg. per kilogram of body weight increased salivary secretion and this action was completely arrested by atropine but not by ethyl yohimbine. As little as 0.001 to 0.01 mg. of privine per kilogram of body weight given intravenously caused retraction of the nictitating membrane, and this effect was partially nullified by either atropine or ethyl yohimbine. It appears that privine possesses both adrenergic and cholinergic actions. C.

Miscellaneous Allergies

Clinical Observations on the Use of Benadryl: A New Antihistamine Substance. McElin, T. W., and Horton, B. T.: Proc. Staff Meet., Mayo Clin. **20**: 417, 1945.

Benadryl, beta dimethylaminoethyl benzhydryl ether hydrochloride, a newly synthesized antihistamine preparation was first studied by Loew and his coworkers. They found that benzhydryl alkamine ethers were effective in preventing fatal histamine or anaphylactic shock in guinea pigs. In the present studies the ability of benadryl to counteract certain of the well-known clinical effects of histamine was investigated. Benadryl was administered orally, intramuscularly, or intravenously. It was found to decrease the vasodilating action of histamine in the skin and nasal mucous membrane. It also decreased the response of the gastric acids and the volume of gastric secretion produced by the administration of histamine. It depressed the wheal and flare response in cases of hypersensitiveness to cold. One hundred twelve patients suffering from a variety of conditions in which the underlying problem seemed to be edema provoked by the local release of histamine or histamine-like substance were treated. They were given benadryl in doses ranging from 50 to 500 mg. per day orally or 20 mg. per injection intramuscularly or from 10 to 120 mg. intravenously by the continuous drip method within a ten-minute period. No evidence of acute toxicity except for mild side reactions was encountered. The reactions consisted of sleepiness, dizziness, dry mouth, nervousness, urinary frequency, fatigue, epigastric distress, vomiting, et cetera. Out of seventy-four patients in whom benadryl was administered orally, fifty-four experienced side effects. Of thirty-eight intravenous administrations of benadryl in twenty-six cases, no side effects were noted in only eight cases. No abnormalities in the erythrocyte, leucocyte, and differential blood counts were observed. The hemoglobin, platelet count, bleeding time, clotting time, and blood urea were not affected by the administration of benadryl. A.

The Use of Benadryl in Treating Some of the Allergic Diseases of Childhood. Logan, G. B.: Proc. Staff. Meet., Mayo Clin. **20**: 436, 1945.

Benadryl in the form of an elixir or in capsules was employed in the treatment of eighteen children suffering from hay fever, asthma, vasomotor rhinitis, urticaria, and serum reactions. The optimum daily dose suggested for children is 2 mg. per pound of body weight divided into from two to four doses. Untoward reactions such as drowsiness and vomiting were noted. In twelve children with seasonal hay fever (ragweed) the administration of benadryl during the season afforded excellent or good results in nine cases, fair in one, questionable in one and no effect in one. In bronchial asthma the administration of benadryl was not as effective. In urticaria and vasomotor rhinitis in children benadryl had a palliative effect. A.

Castor Bean Sensitiveness. Bernton, H. S.: South. M. J. **38**: 670, 1945.

A white male patient, 36 years of age, with a positive personal history of allergy, experienced attacks of paroxysmal sneezing, coryza, lacrimation, itching and swelling of the eyes, and itching of the nose and throat whenever he worked at his carpenter's bench in the basement of his home. Burlap sacks were stored in a basket under his work bench. On one occasion when he used a piece of this burlap for reupholstering a chair, he developed marked coryzal symptoms, wheezing, and urticaria. Scratch tests with all the common foods and inhalants and molds were supplemented by intracutaneous tests. Positive reactions were obtained only with castor bean pomace and burlap slivers from a sack. Positive passive transfer tests were obtained with the nontoxic allergenic fraction isolated from castor bean (CB-1A). A solution of CB-1A diluted 1:1,000,000 in distilled water produced a positive cutaneous reaction on this patient. Quantities of CB-1A as low as 0.000,0001 μg. yielded positive reactions when injected into sites sensitized with 0.05 ml. of the undiluted serum. The uterine horn of a guinea pig previously sensitized to castor bean protein CB-1A contracted when an extract made from the burlap material was added to the Dale bath. The results indicated that the burlap extract contained CB-1A and that the sacks had at one time been in contact with castor bean pomace. Patch tests performed on the patient with castor oil were negative. Castor oil appears to be free of CB-1A. The author cautions against the use of the castor bean plant as a source of insecticides, since it may sensitize predisposed individuals. H.

Streptomycin in Treatment of Clinical Tuberculosis: A Preliminary Report. Hinshaw, H. C., and Feldman, W. H.: Proc. Staff Meet., Mayo Clin. **20**: 313, 1945.

Apparent sensitization to streptomycin was noted in four patients receiving a second course of streptomycin after an interval of several weeks without treatment. The symptoms of sensitization consisted of "violent febrile reactions," which followed the first doses on the resumption of treatment. "Desensitization" permitted continuation of treatment without further ill effects. H.

Allergy and Immunity (Iathergy) in Experimental Tuberculosis. XIII. Intradermal Spread of Vital Dye in Anergic, Allergic, and Iathergic Tuberculous Guinea Pigs. Birkhaug, K., and Berto, E.: Acta. med. Scandinav. **121**: 115, 1945.

Guinea pigs with negative cutaneous reactions to 10 mg. of tuberculin were divided into three groups. Group I (normal-anergic) served as normal controls. Group II (tuberculous-desensitized) was inoculated with 0.0001 mg. virulent human tubercle bacilli and then received subcutaneous injections of 100 mg. crude tuberculin three times weekly. Group III (tuberculous-allergic) was inoculated as in Group II but received no further treatment. Ten weeks later all groups were retested intracutaneously with 10 mg. tuberculin. Group I was negative; Group II showed evidence of almost complete desensitization; and Group III presented strong positive reactions with necrosis.

Animals in all groups then received intracutaneous injections of 0.025 c.c. of pontamine sky blue dye. In Groups I and II there was a very extensive spread of the dye four hours after its injection. At the end of twenty-four hours, the borders of the dy-spread were still detectable in Group III, the mucous membranes showing no evidence of staining. The animals in Groups I and II, however, showed extensive dye-staining of the mucous membranes at this time.

A restricting influence to the spread of a nonspecific, isotonic dye is evidently present in the skin of allergic-tuberculous guinea pigs. The intralymphatic drainage of the dye seems to be slower in this group than in normal or tuberculous-desensitized animals. The intensity of the cutaneous tuberculin reactions was found to be inversely proportional to the spreading-ability of the injected dye. H.

Thrombocytopenic Purpura Following the Use of Sulfathiazole. Strong, P. S., and Glassburn, E. M.: Ann. Int. Med. **23**: 237, 1945.

Thrombocytopenic purpura is an uncommon complication of sulfathiazole administration, only four previous cases having been reported. In the present case, sulfathiazole (19 Gm. in three days) was administered to the patient who was suffering from follicular tonsillitis associated with scarlet fever. Bleeding from the nose and blood in the urine and stool were observed on the fourth day, and the diagnosis of thrombocytopenic purpura was confirmed by blood studies. The authors assume that sulfathiazole was the etiological agent. H.

Treatment of Ménière's Syndrome. Rainey, J. J.: New York State J. Med. **45**: 1753, 1945.

Sixty patients with true Ménière's syndrome were treated by a series of three intravenous injections of histamine phosphate within a four-day period. Fifty-three of these patients suffered from major attacks. Excellent results were obtained in forty-nine cases. Twenty-five per cent of the fifty-three cases had a recurrence of symptoms within from four to twelve weeks. These patients received a second series of treatments and, in some instances, a third.

The author has found this treatment to be simple and relatively safe. H.

Observations on Seventy-Eight Thyrotoxic Patients Treated With Thiouracil. McGavack, T. H., Morton, J. H., Vogel, M., and Schwimmer, D.: J. Clin. Endocrinol. **5**: 259, 1945.

Most of the toxic reactions which were observed during thiouracil treatment disappeared without necessiting an alteration in the course of therapy. They included generalized pruritus in five patients; rashes, most marked over the forearms and legs, in three; edema, most marked about the eyes and around the ankles, in three; and diarrhea in one. Reactions which necessitated cessation of therapy included agranulocytosis in two patients. Two patients experienced chills associated with high temperature, urticara, and "grippe." In each of these patients a subsequent single dose of the drug reproduced the entire syndrome within six hours. This syndrome which is interpreted as being a true hypersensitivity, usually occurs before the tenth day of administration of the drug. Desensitization has not been successful. H.

Precipitin Test for Tuberculin Antibodies. Muether, R. O., and MacDonald, W. C.: J. Lab. & Clin. Med. **30**: 141, 1945.

Old tuberculin was used to coat a suspension of killed bacteria. Blood sera in serial dilutions were shaken with the antigen-coated bacteria and then incubated. The resulting precipitate was extremely fine and granular. Eleven of twelve guinea pigs infected with tubercule bacilli developed precipitin titers in from 1:2 to 1:128 dilution. The sera of eight human beings with positive tuberculin skin reactions gave precipitin titers in dilutions of 1:16 to 1:64. Of eight patients with negative tuberculin skin reactions, only one showed agglutina-

tion. Thirteen patients with active tuberculosis had antibody titers ranging from 1:64 to 1:1024. Twelve patients with arrested tuberculosis had titers of 1:32 to 1:256. E. Kailin.

Simulating Serum-Sickness Reaction to Penicillin. Sullens, W. E.: U. S. Nav. M. Bull. **45**: 752, 1945.

The difficulty involved in determining the agent responsible for an allergic reaction following the therapeutic use of penicillin is demonstrated. A white male, aged 21 years, with an acute gonorrheal urethritis, was treated for three days with sulfathiazole without improvement. The next day penicillin treatment was started, and the patient received a total of 100,000 Oxford units of calcium penicillin in five equally divided intramuscular doses administered at three-hour intervals. The patient became symptom-free. Twenty-three days later following a recurrence of dysuria, a second course of 100,000 Oxford units of penicillin was administered. Six days following the second course of penicillin, the patient developed urticaria over the abdomen, back, and hips, arthralgia of the wrists and ankles, edema of the feet and hands, a temperature of 99° F., headache, and a generalized lymphadenopathy. These symptoms began to subside after three days. Intracutaneous tests were performed on the patient with penicillin one week following the disappearance of symptoms. The patient showed no reaction at the sites of injection, but five hours later multiple small areas of urticaria appeared on the skin of the upper arm above the sites of the skin tests. Similar tests made on three controls were negative. It is concluded from the skin tests that the patient was definitely sensitive to some substance in the solution. A.

Anaphylaxis

Synthetic Benzhydryl Alkamine Ethers Effective in Preventing Fatal Experimental Asthma in Guinea Pigs Exposed to Atomized Histamine. Loew, E. R., Kaiser, M. E., and Moore, V.: J. Pharmacol. & Exper. Therap. **83**: 120, 1945.

Guinea pigs were placed in a chamber fitted to deliver a constant spray of histamine. Under these conditions 80 to 100 per cent of unprotected animals are killed. Protective drugs were then injected intraperitoneally before placing the animals in the chamber. Aminophylline in a dose of 50 mg. per kilogram of body weight reduced the mortality of the guinea pigs 50 per cent and is assigned an activity index of unity. Papaverine, being effective in an amount of 25 mg. per kilogram of body weight, has an activity index of two. The Forneau compounds 929F and 1571F have activity indices of eight and sixteen, respectively. Two benzhydryl ethers each have activity indices of thirty-three. If histamine is given intravenously instead of by inhalation the benzhydryl ethers each have an activity index of sixteen.

The acute toxicity of various preparations was studied on rats and guinea pigs injected intraperitoneally. The LD-50 of 1571F is about two times greater than aminophylline and that of the benzhydryl ethers is about three times greater. E. Kailin.

The Influence of Duration of Sensitization of Anaphylaxis in the Guinea Pig. Winter, L. B.: J. Physiol. **104**: 71, 1945.

Series of guinea pigs were sensitized with horse serum, horse serum albumin, and horse serum globulin. Schultz-Dale studies were done on a uterine horn

excised prior to the portal vein injection of antigen and on the second horn after the injection. A dose of antigen was employed which desensitized the second uterine horn but produced little or no gross anaphylaxis. The tests were done at about thirty-, fifty-, and ninety-day intervals after sensitization. The animals were believed to be more susceptible to anaphylaxis as the time interval increased. The portal vein route for the shocking dose was observed to be more effective in producing gross anaphylaxis than was an injection of antigen into the systemic circulation. This indicates that cells in the liver of the guinea pig are sensitized and that an antigen-antibody reaction in this organ contributes to the gross picture of anaphylaxis. E. Kailin.

Miscellaneous

The Reaction of Products of Initial Stages of Peptic Proteolysis of Human and Horse Serum Albumin With Antisera to the Original Albumins. Kleczkowski, A.: Brit. J. Exper. Path. **26**: 24, 1945.

Human and horse serum albumin were subjected to proteolysis by incubation with commercial pepsin for varying periods of time. At different stages in the process of digestion the products were tested for their ability to precipitate rabbit antisera to human and horse serum albumins. Prolonged peptic digestion modified horse or human albumin so that they failed to react to any extent with antibodies to the original albumins. Before the stage of final digestion, the protein digest loses its ability to be precipitated by the albumin antibodies although it retains its power of specific combination with them since it inhibits the precipitation of unchanged albumins when these are subsequently added. The precipitating power of the protein digest, however, is not lost entirely since precipitation may take place if the concentration of antiserum is increased sufficiently. Two explanations for this phenomenon are offered: (1) The albumin may be changed into products which are still able to combine with antibodies to the original albumin but are not precipitable by such combination. (2) Poorly precipitating and inhibiting digests contain no unchanged albumin but consist of products which form, after combination with antibodies even at optimal proportions, compounds whose solubility is such that precipitation takes place only when their concentration is comparatively high. Precipitability of the digested products can be restored by heating solutions of the products in the presence of salt. A.

Conversion of Non-Precipitating and Inhibiting Protein Complexes Into Forms Again Precipitable by the Antisera to the Original Proteins. Kleczkowski, A: Brit. J. Exper. Path. **26**: 33, 1945.

When one protein is combined with another forming a complex in which one protein is present in excess, the complex fails to precipitate with antiserum to the minor component. Although it still combines specifically with its antibodies. Tomato bushy stunt virus was heated together with serum albumin to form a complex. The complex failed to precipitate the antiserum to the virus. Following peptic hydrolysis of the compound, the virus which was resistant to peptic digestion was recovered in the precipitable form. A complex was also formed between human and horse serum albumin. Since an excess of horse serum was employed, the compound was not precipitable by the antiserum to human albumin. Following incubation of the complex with pepsin under suitable conditions, a split occurred and the resulting components assumed forms which were again precipitable by their respective antisera. This was accomplished despite the fact that both components of the complex are easily affected by peptic digestion. A.

Specific Precipitation of One Protein by Antiserum to Another. Kleczkowski, A.: Brit. J. Exper. Path. **26**: 41, 1945.

Horse albumin was heated in an excess of human or rabbit albumin in various proportions. The resulting complexes were tested for their reactions with antisera to horse and human albumin. The complexes formed between human and horse albumin by heat denaturation were precipitable by the antisera for either albumin. In mixtures in which there was an excess of human albumin the resultant product combined with, but failed to precipitate, antibodies to horse albumin. The same product, however, precipitated antibodies to human albumin. When horse albumin was present in excess over human albumin in the heat denatured mixtures the complex failed to precipitate antibodies to human albumin but combined with them. Products formed by heating antibodies to bushy stunt virus and human or horse serum albumin were precipitated specifically by antiserum to the albumins but not to the virus, although in the latter instance the ability to combine with antibodies was retained. A.

The Effect of Continuous Intravenous Administration of Histamine on Basal Metabolism in Human Beings. Peters, J. A., Horton, B. T., and Boothby, W. M.: J. Clin. Investigation **24**: 611, 1945.

The intravenous administration of histamine produced a rise in the basal metabolic rate in sixteen of twenty-three patients tested. Eleven additional subjects whose basal rate was taken before, during, and after the intravenous injection showed a rise in oxygen consumption which was roughly proportional to the rate at which the histamine was given. The increase in the basal metabolic rate is transitory and drops soon after the drug is stopped. F.

The Staining of Eosinophil Polymorphs and Enterochromaffin Cells in Histological Sections. Lendrum, A. C.: J. Path. & Bact. **56**: 441, 1944.

A dye which scarcely stains erythrocytes, yet colors the granules of the human eosinophile a deep red, is made of crystalline phenol, chromatrope 2R, and distilled water. This is applied for a half hour after the hemalin stain. Even the granular Paneth and enterochromaffin cells of the human intestine are readily distinguishable. The counting of eosinophiles in tissues is thus facilitated. E. Kailin.

Action of Histaminase Preparations in the Heidenhain Dog. Rostorfer, H. H., and Laskowski, M.: Am. J. Digest. Dis. **12**: 337, 1945.

Preparations of a purified histaminase containing at least 1 unit per milligram of protein, were injected intravenously into Heidenhain dogs and, immediately thereafter, 0.82 mg. of histamine dihydrochloride was injected subcutaneously. A second injection of histamine was given either thirty or sixty minutes later. There appeared to be a marked inhibition of the usual effect which histamine produces on the gastric pouch. Further observations showed that the inhibition of secretions was the result of a toxic reaction produced by the histaminase-protein preparation and was not due to the action of the histaminase itself. F.

Allergy Abstracts

Asthma and Hay Fever

Mold Allergy. II. Clinical Analysis. Blumstein, G. I.: Ann. Allergy **3**: 341, 1945.

Forty-one per cent of four hundred and one allergic patients presented positive cutaneous reactions to one or more of thirteen mold extracts used in this study. Twelve clinically sensitive mold patients were identified in this series. Ten of these suffered from asthma, and eight manifested a pollen sensitivity in addition to mold sensitivity. These patients constituted 3 per cent of the entire group or 9 per cent of the group with seasonal symptoms. Complaints referable to the eyes were minimal in most cases with clinical mold allergy. Nasal symptoms, present in each of the twelve cases, constituted the chief complaint in only two. Symptoms were most severe in July and August, when the pollen concentration in the air was lowest and the spore count highest. The molds of etiological significance in this study and those which are recommended for cutaneous testing in patients suspected of being mold-sensitive include *Alternaria, Hormodendrum, Monilia, Helminthosporium, Cephalosporium,* and *Mucor.* Passive transfer tests were positive with the serum of ten of the twelve clinically sensitive patients. The skin-sensitizing antibodies were specific for each mold. Not all patients with seasonal asthma in the period from mid-July to mid-September could be classified in the mold- or in the pollen-sensitive groups. H.

An Auto-Reagin in the Desensitization of Patients With Allergic Diseases. Von Dishoeck, H. A. E., and Klein, S. P.: Acta. med. Scandinav. **115**: 331, 1943.

Studies on the Cooke inhibiting antibody (''anti-reagin'') are presented. During hyposensitization of grass pollen sensitive cases an increase in reagin titer of the serum could be demonstrated before inhibiting antibodies developed. Inhibiting antibodies could be demonstrated in the sera of patients suffering from various allergic diseases with sensitivities to tobacco, orris root, beans, and wheat. In no instance could inhibiting antibodies be found in dust-treated cases despite good clinical results from such treatment. In hay fever patients, both the duration of treatment and the dosage reached were important factors in the development of inhibiting antibody. In sera preserved at 8° C. for one year the inhibiting antibody, like the reagin, suffered little deterioration. Absolute specificity of the inhibiting antibody for its related allergen was noted.

Although high dosage and high inhibiting antibody titers seemed to correlate with good clinical results, satisfactory clinical results were often obtained in hay fever and dust cases in the complete absence of any inhibiting antibody. H.

A Case of Transient Pulmonary Infiltration With Eosinophilia, With Fatal Issue After Treatment by Adrenalin Spray for Asthma. Broch, O. J.: Acta med. Scandinav. **113**: 310, 1943.

Sudden death occurred in a 28-year-old woman within five minutes following the initial use of a 10 per cent epinephrine spray. This patient, who had

had bronchial asthma for one year, was in the hospital with a diagnosis of "transient pulmonary infiltration" and an associated blood eosinophilia of 70 per cent. The symptoms at death were described as those of adrenalin poisoning. It was estimated that not more than from 0.1 to 0.15 mg. of epinephrine had been inhaled and that probably less than this amount reached the alveoli. Epinephrine had been well tolerated a year previously during a tonsillectomy. A reflex reaction resulting in ventricular fibrillation may possibly have been the cause of death. The post-mortem findings in this case are of interest, since autopsy reports in cases of "transient pulmonary infiltration" are uncommon. Although the pulmonary infiltrations originally observed in this patient had disappeared prior to death, microscopic studies of the lungs revealed thickening of the interstitial tissues between the alveoli and infiltration with lymph and plasma cells. In some areas the lung tissue had been completely obliterated and the spaces filled with lymph, plasma, and eosinophile cells. A "great and widespread distribution of eosinophiles" was found in both lungs. The severe edema of the lungs usually reported after epinephrine poisoning was not observed in this case. The post-mortem diagnosis was "subacute inflammation of the lungs." H.

Irreversible Allergy in Non-Tuberculous Diseases of the Chest. Cohen, M. B.: Dis. of Chest. **11**: 236, 1945.

Allergic reactions are divided into two large groups. In Group I are those initiated by nonliving plant and animal foreign proteins and drugs and in Group II, those initiated by living organisms in the infectious diseases. The immediate histologic picture of the reaction in Group I is that of a hive in which the eosinophiles are later replaced by neutrophiles, lymphocytes, etc., at which stage the reaction becomes indistinguishable from other inflammatory reactions. The histologic picture in this group is the same for all antigens and the reactions must, therefore, be regarded as body specific. The allergic reactions in Group II are also inflammatory in nature, but the inflammatory exudate and the histologic picture vary among the different infections such as tuberculosis or syphilis. These reactions are antigen specific in contradistinction to the body specific reactions in Group I. Both types of reactions may be reversible, causing no tissue damage, or irreversible, with tissue destruction and fibrosis. In bronchial asthma both reversible and irreversible allergic reactions may occur together in the same patient. In the cases in which the asthmatic episodes are periodic and there are free intervals between attacks, the reactions are completely reversible and there is no evidence of tissue damage. In intrinsic asthma where the attacks are more frequent and almost constant, allergic reactions occur in areas which have not yet recovered from previous reactions. The chronic inflammatory reactions lead to irreversible changes, tissue death, and scarring and the disease runs a progressively fatal course. A.

The Symptomatic Treatment of Bronchial Asthma and Hay Fever With Benadryl. Koelsche, G. A., Prickman, L. E., and Carryer H. M.: Proc. Staff Meet., Mayo Clin. **20**: 432, 1945.

Eighty-three patients suffering from hay fever or bronchial asthma or both were treated by the oral administration of benadryl in doses of 50 to 100 mg. three times daily. Patients who failed to receive at least 50 per cent relief of symptoms were considered not benefited. Out of the entire group, fifty-seven patients (69 per cent) reported benefit, and twenty-six (31 per cent) reported no benefit. Out of fifty-two cases suffering from hay fever alone thirty-nine patients (75 per cent) reported benefit, and thirteen (25 per cent) stated that

they failed to obtain any relief. In nineteen cases of asthma associated with hay fever, fourteen (74 per cent) reported benefit while five reported none. The results in bronchial asthma alone were much less encouraging. Out of twelve cases, four reported benefit while one reported none. In hay fever patients relief of the nasal discharge and of the irritating feeling in the nose and eyes was noted within sixty minutes after 50 mg. of benadryl was taken. The relief lasted five to eight hours. Protocols of the types of cases treated are not included in the report. The authors fail to state whether any of the patients treated had also received specific therapy and at what period of the pollinating season treatment with benadryl had been instituted. A.

Parenteral Use of Butanefrine on Asthma. A Comparison With Epinephrine. Hartman, M. M.: Ann. Allergy **3**: 366, 1945.

Butanefrine, 1-(3,4-dihydroxyphenyl)-2-amino-1-butanol, is a new sympathomimetic drug which, when administered in twice the dosage of epinephrine, gives equivalent relief in asthma. The advantages of Butanefrine are: (1) it lacks the pressor effect of epinephrine, the diastolic pressure is moderately lowered, the pulse pressure is widened, and there is only slight acceleration of the heart rate; (2) Butanefrine does not cause nausea or vomiting; (3) it does not produce angina in cardiac patients; and (4) tremor and nervousness do not follow its use as frequently as with epinephrine. A comparison was made of the effects of Butanefrine and epinephrine in cases of "extrinsic" (sensitive) asthma with or without infection and in "intrinsic" (infectious) asthma. It was found that Butanefrine 1:500 and epinephrine 1:1000 when injected subcutaneously are equally effective in relieving uncomplicated "extrinsic" asthma. In "intrinsic" asthma, Butanefrine is less beneficial than epinephrine. The vasoconstrictor action of epinephrine limits its own absorption and, therefore, prolongs its effect which is not so in the case of Butanefrine. It is suggested that Butanefrine is much safer for use as a therapeutic trial in asthmatic dyspnea which may be of cardiac origin. A.

Dermatology

Beta Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl) in Treatment of Urticaria. Curtis, A. C., and Owens, B. B.: Arch. Dermat. & Syph. **52**: 239, 1945.

Eighteen patients with various types of urticaria, angioneurotic edema, and dermographism were treated with Benadryl. In eleven of the patients, there was a complete disappearance of urticaria when 50 mg. doses were taken two or three times daily. However, an occasional nonpruritic wheal was sometimes noted. In three cases of chronic urticaria significant improvement was noted, but the symptoms were not entirely controlled even when 100 mg. doses were administered three times daily. In four patients, Benadryl in various doses failed to afford any appreciable relief. Side reactions from Benadryl were observed in three patients. In one of these, weakness and vertigo were so severe that the drug had to be discontinued. The other two patients complained of drowsiness and muscular pains, but one of them continued taking the drug for seven months despite these symptoms. Toxic symptoms were not noted in other patients who took the drug for several months. The administration of Benadryl afforded only palliative relief in chronic urticaria. In acute urticaria, it was effective in aborting the symptoms. **A.**

Use of Benadryl for Urticaria and Related Dermatoses. Shaffer, L. W., Carrick, L., and Zackheim, H. S.: Arch. Dermat. & Syph. **52**: 243, 1945.

Benadryl was found to be effective in the relief of seven of eight cases of urticaria. In chronic urticaria, it was employed as a palliative measure during the period of investigation. In acute urticaria, a few doses were usually sufficient to abort the attack. In one case of lichen urticatus with urticaria and erythema multiforme, symptomatic relief occurred after six doses of 50 mg. of Benadryl. One patient with atopic eczema was completely relieved of pruritis and the skin lesions were markedly improved after the administration of 50 mg. four times daily for five weeks. Benadryl appeared to be without effect in the treatment of neurodermatitis or dyshidrotic eczema. Benadryl produced no untoward effects in this series of cases. A.

Benadryl in the Treatment of Urticaria. O'Leary, P. A., and Farber, E. M.: Proc. Staff. Meet., Mayo Clin. **20**: 429, 1945.

Fifteen patients suffering from acute urticaria and thirty-five patients with chronic urticaria were treated by the oral administration of benadryl. The dosage varied from 50 to 100 mg. two to five times a day. Nine out of the fifteen cases of acute urticaria experienced prompt relief consisting of a decrease or disappearance of pruritus in from twenty to sixty minutes after the initial dose. The lesions disappeared within two to six hours. Five patients showed some improvement and one failed to receive any benefit. Among the thirty-five patients with chronic urticaria (average duration four years) twenty-five experienced a disappearance of the lesions except for the occasional presence of a few nonpruritic hives, seven patients were improved, and three were not benefited. In all but one patient there was a prompt recurrence of urticaria when placebos were substituted or when administration of benadryl was discontinued. Benadryl appears to be a palliative rather than a curative measure in the treatment of urticaria. Eighteen out of fifty patients in the series experienced toxic symptoms from the ingestion of benadryl. These consisted of drowsiness, dizziness, weakness, dilated pupils, and dry mouth. These symptoms abated in some patients when the dose was diminished or after the drug had been administered for several days. Three out of the eighteen patients who experienced reactions were forced to discontinue the drug because of the severity of the symptoms. A.

Contact Dermatitis of Eyelids Caused by an Antioxidant in Rubber Fillers of Eyelash Curlers. Report of Seven Cases. Curtis, G. H.: Arch. Dermat. & Syph. **52**: 262, 1945.

Seven cases of contact dermatitis of the eyelids in women showed certain distinct characteristics which distinguished them from other common eruptions on the eyelids. The dermatitis was subacute and showed no vesiculopapules. The dermatitis was bandlike with well-defined borders and there was a narrow band of normal skin between the borders of the dermatitis and the margin of the lid. When the dermatitis involved most of the cutaneous surface of the upper lids, a narrow band of normal skin along the tarsal fold tended to divide the dermatitis into two bands. The lesions were found to be caused by the rubber fillers of an eyelash curler.

Patch tests were performed on five patients with rubber fillers and with the ingredients of rubber fillers, namely 5 per cent sulfur in petrolatum, 5 per cent lead oleate in petrolatum, zinc oxide powder, and a petrolatum control. Diphenyl guanidine (0.25 per cent) which was present in the filler as an accelerator and phenyl-beta-naphthylamine which was employed as an antioxidant were also tested at a later date. Positive reactions were obtained in five cases

with phenyl-beta-naphthylamine from one to four years after the original patch tests with the rubber fillers were made. Two patients were not available for the more recent studies. Two patients in the series showed positive reactions to patch tests with ordinary rubber bands and with the rubber of hose supporters. A.

The Destruction by Tyrosinase of the Irritant Principles of Poison Ivy and Related Toxicants. Sizer, I. W., and Prokesch, C. E.: J. Pharmacol. & Exper. Therap. **84**: 363, 1945.

Mushroom tyrosinase catalyzes the oxidation of the dermatitis-producing compounds of poison ivy. Patch tests performed with the material thus oxidized in vitro showed partial inactivation of the active agent. A mixture of antigen and tyrosinase placed on the skin resulted in a lesser degree of dermatitis than that produced by a control solution. Similarly a tyrosinase-soaked gauze patch placed on areas which had been exposed to poison ivy oleoresin from four to twelve hours previously, diminished the amount of dermatitis which developed on these sites. No studies were done on lesions which had already appeared. E. Kailin.

A Note on the Statistical Probabilities of Finding Hypersensitive Subjects in Random Samples. Knudsen, L. F.: J. Invest. Dermat. **6**: 231, 1945.

The author offers an equation for estimating the probability of obtaining no patch test reactors, one reactor, or more than one reactor in a sample of a specified number of subjects when the population rate is the known factor. As an example, the author demonstrates that, when an infinite number of homogeneous groups (each group consisting of two hundred subjects) are tested with a substance which is known to have a positive reaction rate of 0.1 per cent for the population, 82 per cent of the groups would have no reactors, 16 per cent of the groups would have one reactor, and about 2 per cent of the groups would contain more than one reactor. A.

Urticaria From Perfume. Zakon, S. J., and Kahn, J. B.: Arch. Dermat. & Syph. **52**: 11, 1945.

The patient, a 45-year-old white housewife, had had recurrent urticaria for six years which had failed to respond to dermatologic and allergic therapy. The personal history was negative for other forms of allergy. The patient used perfume and scented cosmetics constantly and submitted a list of forty-eight different perfumed preparations which she employed. In view of the negative physical and laboratory findings, the patient was advised to remove all traces of perfume from her clothing, to use unscented cosmetics, and to keep away from persons using scent excessively. Within one week following the institution of this regime, the hives disappeared. Shortly thereafter, following contact with several women who were users of perfume, she had a recurrence of the urticaria. The complexity of the chemistry of perfumes is discussed. Patch testing with perfumes is of little value in view of the wide variety of materials which are employed in their manufacture. Perfume must be considered as a causative agent in allergic diseases and may act either as a contactant or as an inhalant. A.

Boric Acid: A Dangerous Drug of Little Value. Watson, E. H.: J.A.M.A. **129**: 333, 1945.

A child, 4½ months of age, suffering from infantile eczema, developed a temperature of 102° F. twenty-four hours following the institution of boric

ointment applications. Shortly after this, convulsions occurred and the temperature rose to 107° F. Within the next few days, a characteristic intense erythema, the color of a boiled lobster, was noted. Death ensued about three weeks after the onset of the reaction. It is strongly recommended that the use of boric acid preparations be discontinued. F.

Recurrent Herpes Simplex. Shulman, B. H.: U. S. Nav. M. Bull. **45**: 161, 1945.

A case of recurrent herpes simplex in which sunburn was a predisposing factor is described. The patient, a white man, aged 21 years, showed pruritic vesicles on the cheek, paranasal, infra-orbital, and temporal regions, all on the right side. At the age of 3 years, he had sustained a burn of the right malar eminence. Thereafter, he had from one to three attacks of a peculiar facial eruption each summer. These persisted from seven to fourteen days and always involved the site of the previous burn. Moderate exposure to the sun usually precipitated an attack within three or four days. The rash was accompanied by conjunctivitis and photophobia of the right eye. The family history was negative for allergy or herpes. These recurrences may be the result of local skin sensitization or they may be recrudescences of a latent persistent herpes simplex infection or a combination of these factors. A.

Sensitivity to Local Applications of Sulfanilamide. Taubenhaus, L. J.: Surgery **15**: 483, 1944.

Vesicular dermatitis following sensitization by continuous application of sulfanilamide powder to small surface wounds was observed in three cases. Inhibition of the epithelization of the wounds was noted in these patients. This potential danger of local sulfa therapy is stressed. H.

Rubber Products as Widespread Cause of Eczema. Report of 80 Cases. Bonnevie, P., and Marcussen, P. V.: Acta. dermat.-venereol. **25**: 163, 1944.

Rubber dermatitis is believed to be more common than has previously been suspected. The eighty cases here reported represent 2 per cent of the total number of contact dermatitis cases observed. Twenty-five of them could be classified as occupational dermatitis. Seventy-four per cent of the eighty cases had their contact with rubber in footwear or articles of clothing. Eruptions of the feet caused by rubber sensitivity are frequently difficult to distinguish from mycotic eczema. Rubber was found to be subordinate in etiological importance to the accelerator agents, especially mercaptobenzothiazole which proved to be the most common agent of sensitization. In those cases where only accelerator hypersensitivity was present, cold-vulcanized rubber could frequently be tolerated. H.

Otorhinology and Ophthalmology

Allergic Retinosis. Bettman, J. W.: Am. J. Ophth. **28**: 1323, 1945.

Allergic retinosis was observed in a 42-year-old man who gave a history of having had hay fever and occasional attacks of asthma since the age of 15. The family history was strongly positive for allergy. For two years, there had been attacks of itching, burning, and tearing of the eyes. Examination revealed injection of the conjunctivae and opacification of the corneae. A few eosinophiles were found in a smear taken from the left eye. Intracutaneous

tests showed positive reactions to a number of foods and inhalants. Polyps were present in the nose. During an exacerbation of the nasal symptoms, vision in the right eye became progressively blurred. On ophthalmic examination, an area, which appeared to be edematous, was noted temporally and below the optic disc. This area was white and slightly elevated. The edema was most marked below the fovea. The remainder of both fundi was normal. One-half hour after the administration of 1 c.c. of adrenalin, the visual acuity had improved and the edema had diminished. After two days of a low salt diet and daily injections of epinephrine in oil, fundus examination showed the edematous area to have cleared almost completely. Allergic reactions on the retina may be manifested by edema, hemorrhages, and retinal detachments. C.

Ocular Sensitivity to Butyn. Esposito, A. C.: Am. J. Ophth. **28**: 1362, 1945.

Ocular sensitivity to 2 per cent butyn sulfate solution was manifested by conjunctivitis and edema of the lids. The reaction was observed two to three hours following the instillation of the anesthetic into both eyes. A patch test performed with butyn sulfate was markedly positive within forty-eight hours after the application. Only four similar cases have been recorded in the literature. C.

Miscellaneous Allergies

Hypersensitivity to Iodine as a Cause of Periarteritis Nodosa. Rich, A. A.: Bull. Johns Hopkins Hosp. **77**: 43, 1945.

A fatal case of periarteritis nodosa is presented. The patient was admitted to hospital with symptoms, signs, and laboratory findings of hyperthyroidism. Iodine therapy was instituted. The patient died three weeks later. Itching of the skin, a papular rash, coryza, painful joints, and eosinophilia up to 22 per cent developed before death.

Microscopic lesions characteristic of periarteritis nodosa were found in the visceral organs. The lesions involved the small arteries mainly, and consisted of smudgy or hyaline necrosis of the media of the segment or of the entire circumference of the artery. They showed perivascular infiltration of mononuclear leucocytes and eosinophiles. The thyroid gland showed marked hyperplasia with some areas of involution.

Iodine is now added to the list of sensitizing substances that may cause periarteritis nodosa. The author believes that iodine, like the sulfonamides, may act as an antigen by conjugation with plasma proteins. If the sensitizing antigen in periarteritis nodosa can be identified it may be possible to prevent progress of the condition either by eliminating contact with the antigen or by desensitization. J. Sherman.

Tropical Eosinophilia as Seen in England. Apley, J., and Grant, G. H.: Lancet **1**: 812, 1945.

Among one hundred and fourteen consecutive chest cases sent back to England from the East, five cases of tropical eosinophilia were encountered. In the entire group only these five cases showed a pronounced blood eosinophilia. Ninety-six cases of bronchitis or asthma or both were in this group. Eosinophilia in combination with pulmonary lesions occurs in Löffler's syndrome, tropical eosinophilia, periarteritis nodosa, bronchial asthma, and some intestinal infestations. The distinction between tropical eosinophilia and Löffler's syndrome is not sharp and it is best to consider both as manifestations of one type of disease process. The E. P. syndrome (eosinophilia-pulmonary) is probably the end result of similar processes not necessarily evoked by the

same agents. Whether tropical eosinophilia is caused by specific arsenic-sensitive organisms or whether it is an allergic response common to a variety of allergens has not been determined. Mites have been implicated as a cause of the E. P. syndrome but their etiological importance has not been proved. In the differential diagnosis between tropical eosinophilia and Löffler's syndrome the point is frequently made that Löffler's syndrome occurs in dry climates whereas tropical eosinophilia originates in humid climates. Intestinal infestation as a cause of the E. P. syndrome is rare. Bronchial asthma forms the largest group among cases showing the E. P. syndrome. Associated with the asthma, transitory pulmonary infiltrations and pleurisy with marked eosinophilic effusions, have been observed. Transitory pulmonary infiltration associated with a high blood eosinophilia also occurs in periarteritis nodosa. Extensive laboratory studies should be made to exclude other conditions before a diagnosis of tropical eosinophilia can be entertained. Treatment with arsenic is indicated even if the diagnosis of tropical eosinophilia is only tentative. The response to arsenotherapy is highly satisfactory. **A.**

Ether Allergy: A Case Report. Stein, H. B.: Anesthesiology **6**: 515, 1945.

Circulatory collapse occurred in a 20-year-old man who was receiving ether anesthesia prior to a laminectomy. Sodium amytal and seconal had been administered the previous night and nembutal, morphine, and scopolamine were given an hour before the operation. Ethyl chloride induction was used by the open drop method and then ether was administered using the same mask. Slight cyanosis was noted as soon as ether was started but this cleared up when oxygen was given. When the ether mask was reapplied, the patient again became cyanotic and oxygen was administered through an endotracheal tube. Despite this the patient went into circulatory collapse with complete absence of pulse. The respirations remained full and moderately rapid. Various types of emergency therapy were employed and after two hours the patient's condition improved. At this time scopolamine sensitivity was blamed for the reaction. About four hours after the anesthetic had been discontinued the patient's hands and eyes became moderately edematous and his temperature rose to 103° F. He complained of itching of the entire body. Six days later laminectomy was performed under spinal anesthesia. A sudden fall in blood pressure was noted after ether had been applied to the skin preceding the application of tincture of iodine. The true nature of the reaction was not recognized until the patient casually remarked that "when ether is used on me to remove adhesive it burns, then itches and hives appear." Several weeks after the laminectomy a few drops of ether were poured on the forearm as a test for hypersensitivity. Within two or three minutes burning and itching were complained of and soon a giant wheal developed. Passive transfer studies were performed. Two-tenths of a cubic centimeter of the patient's serum was injected intracutaneously in the back of a normal subject. Twenty-four hours later, ether was applied to this area and within a few minutes a giant wheal with a surrounding zone of erythema appeared. At no time during the administration of the ether to the patient had there been any evidence of respiratory difficulty suggestive of pulmonary edema or asthma. The possibility that the entire reaction might have been a manifestation of a physical allergy to cold was not discussed. **A.**

The Allergen of House Dust. Sutherland, C.: M. J. Australia **1**: 583, 1945.

A polysaccharide-containing fraction was isolated from house dust by adsorption of an aqueous extract on benzoic acid. The adsorbed material was dried and dissolved in water. After centrifugation, the clear supernatant fluid was precipitated with acetone. The purified material showed greater

activity than the original adsorbate and gave no reactions for proteins. It was soluble in phosphate-buffered saline solution and lost a good deal of activity when it was Seitz filtered. Scratch and intracutaneous tests performed with adsorbed fraction of house dust on a large series of subjects indicated that the fraction was highly active and was nonirritating. For therapeutic desensitization, a 1:10,000 dilution was employed at the start. It was usually possible to reach a final dose of 1 ml. of a 1 per cent solution. Treatment with house dust adsorbate alone seemed to be effective in patients who had multiple sensitivities to various inhalants but in whom the associated sensitivities were not pronounced. In a group of one hundred patients sensitive to house dust, there was no constant association of dust sensitivity with any other allergen. The author believes that house dust contains some unique allergen. All patients who showed positive scratch reactions with ordinary house dust extract showed larger reactions to the more refined adsorbed fraction. **A.**

An Unusual Effect of Aminophylline on the Intestinal Tract. Zeller, M.: Ann. Allergy **3**: 369, 1945.

Aminophylline given intravenously for the treatment of asthma in a 42-year-old woman not only relieved the asthma but apparently also relieved severe painful abdominal distention. The patient gave a history of bronchial asthma and hay fever of fifteen years' duration, intestinal distention, attacks of nausea and vomiting for eighteen years, and frequent headaches. She had had an appendectomy and a cholecystectomy without relief of her abdominal symptoms. Two additional laparotomies performed for intestinal obstruction failed to improve her chronic intestinal disturbances. Ingestion tests with a number of foods produced abdominal distention and pain. The intravenous injection of 7½ grains of aminophylline repeatedly relieved severe attacks of abdominal distention and pain and on one occasion produced complete relief of acute intestinal obstruction. Roentgenograms taken before and after the injection of aminophylline showed the antispasmodic effect of the drug on the bowel. The author suggests that intravenous aminophylline is a valuable measure in the differential diagnosis between the acute surgical abdomen and the allergic bowel. **A.**

Serum Incompatibility as Cause of Transfusion Accident. Pryor, G. A. W., and Singer, E.: M. J. Australia **1**: 588, 1945.

An allergic reaction to plasma constituents was observed in a patient who had received repeated transfusions with bloods from different donors. The patient had noticed a tendency to bleed spontaneously after small cuts. He had been exposed to acetone, ethyl formate, and toluene. He gave no history of allergy. He showed no reaction after the first transfusion of 500 ml. of citrated blood. Five days later, shortly after a second transfusion by the direct technique, his temperature rose to 101.7° F., and he complained of headache, joint pains and chilliness. Before the third transfusion the blood of the recipient and that of the new prospective donor were tested for incompatibility. No agglutination was observed. However, when diluted serum of the donor was layered over the serum of the patient, a faint but clearly marked ring of precipitation developed after fifteen minutes' incubation. When citrated blood from this donor was given by the drip method, the patient's temperature rose to 104° F. within thirty minutes and the transfusion had to be stopped. The patient's sensitivity could be passively transferred to the skin of a normal

subject. When the sensitized sites were tested with the sera of various donors positive reactions were elicited. They showed reactions with the blood of ten donors. A.

Periarteritis Nodosa. A Case With Autopsy. Washburn, R. N., and Otto, T. O.: Am. J. M. Sc. **210**: 640, 1945.

A 21-year-old soldier with a past history of seasonal hay fever became ill with pain in the right upper quadrant of the abdomen, a mild fever, anorexia, and weakness. Examination revealed an indefinite mass in the right upper quadrant. The blood study showed a moderate secondary anemia and slight elevation of the white blood count with 88 per cent neutrophiles but no eosinophiles. A laparotomy revealed enlargements of the liver, spleen, and gall bladder. A cholecystectomy was performed. Signs of cardiac failure developed on the seventh postoperative day and the patient died two days later.

On microscopic examination extensive visceral vascular lesions which were confined to the medium-sized arteries and affected mainly the adventitia suggested the diagnosis of periarteritis nodosa. The vascularity and extensive inflammatory exudate with moderate fibrosis of the vessel walls indicated an early stage of the disease. J. Sherman.

Use of Benadryl in the Syndrome of Physical Allergy of the Head: A Preliminary Report. Williams, H. L.: Proc. Staff. Meet., Mayo Clin. **20**: 434, 1945.

The syndrome of "physical allergy of the head" consists of the related conditions of perennial vasomotor rhinitis, myalgia, endolymphatic hydrops (Ménière's disease) and vasodilating pain. These conditions are said to depend on physical or intrinsic allergy and are not mediated by an antigen-antibody type of reaction. They appear to be due to a release of histamine. Patients with physical allergy of the head could be maintained relatively free of symptoms by the oral administration of 300 mg. of benadryl given in six equally divided doses at intervals of two hours from morning until night. Relief of symptoms from 50 mg. of benadryl began in half an hour and continued for about two hours. Twelve patients with perennial vasomotor rhinitis were treated. Ten obtained 90 per cent relief, and two obtained no relief. The two who experienced no relief experienced such extreme dizziness after taking 50 mg. of benadryl that they discontinued treatment. Four patients with hyperplastic ethmoiditis obtained marked symptomatic relief with a retraction and disappearance of polypoid tissue and a diminution or disappearance of purulent discharge. Symptoms recurred within twelve hours after the discontinuance of benadryl. Five patients with myalgia of the head reported greater relief from the use of benadryl than from niacin. In Ménière's disease patients experienced more relief from the administration of a combination of niacin and potassium nitrate than from benadryl. A.

Polyneuritis After Treatment With Sulfonamide Preparations. Bruun, E., and Hermann, K.: Acta. med. Scandinav. **111**: 261, 1942.

Sixteen cases of polyneuritis following sulfonamide therapy are reported. Eleven cases occurred with sulfamethylthiazole, two with sulfathiazole, one with sulfanilamide, one with sulfapyridine, and one with uliron. No relationship was observed between the amount given and the severity of the polyneuritis. In four cases, the complication appeared during the course of the treatment and in twelve it occurred from one to three weeks after the therapy had been discontinued. The neuritic disturbances had disappeared within ten months in the majority of cases but were still present in one case after two years. H.

Anaphylaxis

A Commentary on Our Knowledge of the In-Vitro Anaphylactic Reaction With Tuberculin. Groenwall, A.: Acta med. Scandinav. **116**: 470, 1944.

The tuberculin molecule is chemically a complex. PPD (Seibert) and PPD (Standard) are the purest available forms of tuberculin, containing only small amounts of impurities (nucleic acid and polysaccharide). These purified tuberculins are homogenous according to ultracentrifuge studies. Two fractions can be seen in electrophoretic experiments. The various types of reactions observed with tuberculin may be due to various parts of this highly complex protein substance.

The uteri of guinea pigs, sensitized with 0.1 mg. virulent human tubercle bacilli, were tested by the Dale technique for anaphylactic sensitivity with tuberculin Schubert, PPD Seibert, and PPD Standard. Specific uterine contractions could be obtained with tuberculin Schubert but both PPD tuberculins gave negative results. In some instances, tuberculin Schubert produced specific uterine contractions following negative reactions to PPD preparations. It should be noted that PPD is prepared from old tuberculin, while tuberculin Schubert is prepared from the culture medium. H.

Experiments for the Further Clarification of Allergic Bronchial Asthma (Experiments With Goat and Eel Sera). Kallós, P., and Kallós-Deffuer, L.: Acta. med. Scandinav. **116**: 409, 1944.

Anaphylactoid symptoms may be produced in guinea pigs by the inhalation of beef, hog, goat, or eel serum. The primary toxic effects of goat and eel sera were studied in detail. In guinea pigs, the inhalation of goat serum produces, within a few minutes, an increased blood and tissue eosinophilia, especially peribronchial. At the height of the reaction, which resembles anaphylaxis, the lungs are large, distended, white, and dry on section. The bronchi, filled with mucus containing eosinophiles, are apparently occluded since it is impossible to instill lipiodol into the lung through the trachea. Following the inhalation of eel serum pulmonary hemorrhages may be found throughout the lung within a few minutes. Few eosinophiles are present. Bronchial spasm is absent. At the height of the reaction, which clinically is similar to that observed in the goat-serum-treated animals, the lungs are of normal size, blue black in color, and hemorrhagic. Similar results to those produced by inhalation are obtained with both goat and eel serum administered intravenously. The authors conclude that eel and goat sera contain primary toxic substances, which behave differently. The toxic substance in goat serum acts on smooth muscle and that in eel serum on the blood vessel.

Aminophylline or theamin injected intravenously into sensitized guinea pigs just prior to the shocking dose inhibit shock symptoms. Good results are also reported when aminophylline is injected at the height of the anaphylactic reaction. The toxic action of goat serum in guinea pigs is inhibited by the intravenous administration of aminophylline. Indefinite results are obtained when eel-serum-treated animals are given aminophylline. It seems, therefore, that aminophylline has a decidedly greater effect on bronchial smooth muscle than on the vascular structure. H.

The Effect of a New Adrenalin Preparation on Experimental Asthma. Kallós, P., and Kallós-Deffuer, L.: Acta. med. Scandinav. **116**: 441, 1944.

Adrenalin with an excess of ascorbic acid, prepared in a lipoid mixture, was suggested by A. Kennedy in 1941 for intramuscular use in asthma. This

mixture has an action which persists six hours and produces no side effects. This "adrenalin-retard" was tested in guinea pigs exposed to histamine inhalations. Injections of "adrenalin-retard" inhibited histamine intoxication in these animals for longer than six hours. Intramuscular injection produced only slight round cell infiltration at the site of injection. H.

Miscellaneous

Eosinophilia in Silicosis. Habeeb, W. J.: Am. Rev. Tuberc. **52**: 337, 1945.

Examination of the records of a group of male patients admitted to a tuberculosis sanitarium during a recent two-year period revealed that a high percentage of them manifested an unexplained eosinophilia. One hundred and thirty-four of the patients studied were coal miners and five hundred and eighty-two were nonminers. Some of these patients had tuberculosis, some had silicosis, while others had silicotuberculosis. Eosinophilia occurred in 51.2 per cent of the coal miners suffering from silicosis and in 32.4 per cent of the miners with silicotuberculosis. On the other hand, only 16.1 per cent of the miners with tuberculosis and 5.9 per cent of the nonminer group of patients showed an eosinophilia. It was further noted that the degree of eosinophilia was proportional to the extent of the silicosis and the resultant emphysema. Because silica and coal dust are inert materials and are not likely to produce a generalized allergic response, it is suggested that the eosinophilia is the result of alveolar distention and of the expiratory delay produced by the emphysema. F.

Anaphylactoid (Sanarelli-Shwartzman) Reaction Following Therapeutic Antityphoid Injections. Love, J., and Driscoll, R. H.: U. S. Nav. M. Bull. **45**: 1104, 1945.

A 20-year-old white man suffering from choroiditis of the left eye was given 0.1 c.c. of vaccine (100 million organisms) antitriple typhoid intravenously. The patient's temperature rose to 102° F. in twelve hours and dropped to normal within three hours. Twenty-four hours later a second dose of 0.1 c.c. of the vaccine was administered intravenously. Within an hour the temperature rose to 102.6° F. and the patient had a severe chill. Shortly thereafter the pulse rate rose to 160 and the axillary temperature was 107.2° F. In the next twenty-four hours, the temperature and pulse rate dropped and the patient was given a transfusion of 1,000 c.c. of whole citrated blood. The next day the patient's temperature was normal and his general condition was greatly improved. Several hours later, he vomited a dark brown fluid which appeared to be blood. The patient was catheterized and a small amount of dark brown urine was obtained. A blood urea nitrogen determination at this time showed 66 mg. per 100 c.c. of blood. Within the next few hours the patient became disoriented and had repeated attacks of hiccups. He died rather suddenly the next day. At autopsy, there were generalized petechiae throughout the parenchymal organs and brain. There was also massive necrosis of the liver and kidneys. Death was attributed to a generalized anaphylactoid reaction similar to that described by Sanarelli and Shwartzman in experimental animals. Sanarelli produced the Shwartzman phenomenon on a generalized scale by administering the preparatory and provocative injections intravenously. The writers believe that reactions of this nature can be avoided if an interval of forty-eight hours is allowed to elapse between injections of typhoid vaccine. The literature on untoward reactions following the administration of typhoid vaccine is reviewed. A.

Allergy Abstracts

Asthma and Hay Fever

Observations on Loeffler's Syndrome. Report of Four Cases. Blanton, H. W.: Virginia M. Monthly **72**: 437, 1945.

Four cases of Löffler's syndrome were observed and studied. The familial aspect of the syndrome is stressed. In two cases both a father and daughter who suffered from bronchial asthma later manifested transient pulmonary infiltrations. Eosinophilia which is commonly associated with Löffler's syndrome may sometimes be absent. The author believes that Löffler's syndrome is an allergic reaction to various allergens which may be difficult to identify. Intestinal parasites may be offending allergens. In three of the cases studied, x-rays of the chest were made before and one hour after a subcutaneous injection of adrenalin was administered. A complete disappearance of the pulmonary infiltration was noted after the injection. The next day the shadows reappeared, and subsequent injections of adrenalin often failed to clear the lung shadows. The response to adrenalin is regarded as confirmatory evidence of the allergic nature of Löffler's syndrome. A complete review of the literature and a discussion of the etiology and pathology of the syndrome is included in the report. A.

Streptomycin Aerosol in the Treatment of Chronic Bronchiectasis: Preliminary Report. Olsen, A. M.: Proc. Staff Meet., Mayo Clin. **21**: 53, 1946.

In nine cases of chronic bronchiectasis where penicillin aerosol had failed to produce improvement, streptomycin aerosol was successful in the eradication of numerous gram-negative organisms and in the diminution of the volume of sputum. The author recommends combined penicillin and streptomycin nebulization to be used as preoperative therapy for pulmonary resection and as a temporary measure for nonsurgical bronchiectasis. E. Walzer.

Loeffler's Syndrome (Transient Pulmonary Infiltration With Eosinophilia). Spector, H. I.: Dis. of Chest. **11**: 380, 1945.

A case of Löffler's syndrome in a 44-year-old man is reported. The family history was negative for asthma and tuberculosis. In the past history a cough of a year's duration had been relieved in four different occasions by the removal of nasal polyps. For one month the patient complained of chills, fever, anorexia, weight loss, and cough. There was mild cyanosis of the lips and finger tips. Dullness was elicited in both axillae and over the right apex, and râles were heard at the right base. There was a leucocytosis of 11,200 with eosinophilia of 29 per cent. Radiographic studies showed changing infiltrations of the lungs which cleared within a month.

After this episode, the patient developed bronchial asthma which followed local treatment of his nasal condition. The author assumed that the patient was allergic to the drugs employed in the nasal therapy. He concluded that an "allergic background prepared the soil for the development of the eosinophilic pneumonitis." E. Walzer.

The Treatment of Bronchiectasis With Chemotherapy and Allergy Management. Thomas, J. W., Van Ordstrand, H. S., and Tomlinson, C.: Ann. Int. Med. **23**: 405, 1945.

Forty-eight per cent of one hundred and ninety consecutive cases with bronchiectasis gave a history of major allergy of the respiratory tract. Fifty-five of the present series of seventy-five cases had associated major allergies including bronchial asthma, "perennial allergic bronchitis," and severe perennial allergic rhinitis. Dramatic results were obtained following the oral administration of 7.7 grains of sulfadiazine, four times daily for four weeks. Such courses of treatment were repeated one to nine times in twenty-three patients. Twenty-one cases were treated solely by allergic management with good results in many cases. Satisfactory results were also obtained in thirty-eight cases, treated with sulfonamide therapy combined with allergic management. Recurrences were noted especially following upper respiratory infections, the cessation of allergic management, and inadequate sulfonamide therapy. Postural drainage, rest, diet, vitamins, and sinus treatments were part of the general treatment. H.

Reactions Following Bronchography With Iodized Oil. Mahon, G. S.: J. A. M. A. **130**: 194, 1946.

Fatalities following the use of iodized oil in the bronchial tree are rare. Reactions such as swelling of the parotid and submaxillary glands, asthma, urticaria, and dermatitis are not uncommon. The author reports the case of a 41-year-old man who died more than one hour after intrabronchial instillation of lipiodol. The patient had given a history of slight cough but there was no history of asthma. Post-mortem findings, however, were highly suggestive of asthma as the cause of death. The bronchi and bronchioles were filled with thick inspissated mucus. Eosinophiles were found in the secretions and in the mucosa and submucosa of the bronchioles. F.

Dosage of Ephedrine in Bronchial Asthma and Emphysema. Herxheimer, H.: Brit. M. J. **1**: 350, 1946.

The effect of the size of the dose of ephedrine was studied in a group of sixty-five patients suffering from bronchial asthma with or without emphysema. Fourteen cases of mild asthma responded favorably to small doses. Of the remaining fifty-one patients, fourteen were severe asthmatics of the extrinsic type and thirty-seven had emphysema with or without a preceding history of bronchial asthma. The patients in this series reacted to ephedrine in various ways. Five responded well to doses of less than 1 grain three times a day. Three were hyperresponsive to very small doses. Twenty-eight needed doses as high as 3½ grains three times a day before satisfactory results were obtained. Eight were refractory, failing to respond to doses as high as 3 or 4 grains three times a day. Effective doses of ephedrine resulted in an average increase of 518 ml. in the vital capacities of the patients in this series. An increase of 200 ml. in the vital capacity was usually accompanied by easier breathing and a decrease in dyspnea. Acquired tolerance to ephedrine occurred in some patients after three or four days. Higher dosage then proved satisfactory. Toxic symptoms often appeared on the first day of treatment, but these were usually mild and disappeared spontaneously with continued use of the drug. In those who acquired a tolerance to large doses, discontinuation of the drug for three or four days resulted in a restoration of responsiveness. The best results were obtained by giving the ephedrine for three or four days and allowing an interval of three or four days before readministration. F.

Bronchoscopy as an Aid in the Diagnosis and Treatment of Allergic Pulmonary Disease. Lell, W. A.: Arch. Otolaryng. **43**: 49, 1946.

Organic changes in the tracheobronchial tree or esophagus may cause asthmatoid symptoms independently of allergic factors, and these should be ruled out by bronchoscopy in all cases of asthma. Of one hundred and seventy-six children examined bronchoscopically because of symptoms of asthma, eighteen had foreign bodies in the respiratory tract, five had foreign bodies in the esophagus, and twenty-three had other organic changes. The results of two hundred and sixty-nine bronchoscopic examinations performed in one hundred and two patients in status asthmaticus are presented. The pathologic findings were uniformly consistent and were characterized by hemorrhagic and redundant mucous membranes which greatly reduced the caliber of the tracheal and bronchial lumen. Thick tenacious secretion was always present and there was always collapse of the posterior tracheal wall on expiration. The changes were confirmed in the gross and microscopic studies of the respiratory tracts of five patients who died in status asthmaticus. C.

Recovery From Pulmonary Moniliasis Following Serum Therapy. Hiatt, J. S., Jr., and Martin, D. S.: J. A. M. A. **130**: 205, 1946.

A patient with severe pulmonary moniliasis failed to respond to the usual treatment with iodides and intravenous gentian violet. Skin tests and agglutinin reactions with *Candida albicans* were negative. An intracutaneous test with anti-*Candida albicans* rabbit serum produced a wheal with pseudopodia and erythema. A control test with normal rabbit serum was negative. Treatment with subcutaneous doses of anti-*Candida albicans* rabbit serum was instituted. Dramatic recovery ensued. Following recovery, the agglutination test for *Candida albicans* was positive in the 1:80 dilution. At this time the immune rabbit serum gave a reaction no larger than the control. The skin test with the fungus extract was slightly positive on one occasion but became negative within a short time. F.

Dermatology

Studies in Hypersensitivity to Light. I. Preliminary Report. Sulzberger, M. B., and Baer, R. L.: J. Invest. Dermat. **6**: 345, 1945.

A case of true urticaria solaris in a white man aged 30 years is reported. For the past ten years the patient had noticed that he developed hives and itching on areas of the skin exposed to sunlight and that exposure to diffuse daylight caused erythema and itching. Experimental exposure of the skin to irradiation with an Alpine lamp produced a wheal which was sharply confined to the area of direct exposure. A margin of erythema surrounded the wheal. By the use of filters it was determined that the upper limit of the patient's urticarial sensitivity to light was between 3,900 and 3,300 A units and the lower limit was below 2,500 A units. This explained why the skin also reacted to Alpine radiation filtered through window glass, although the reaction was much weaker. Window glass filters out all radiation below 3,200 A units. Sites passively sensitized with the patient's serum reacted to sunlight and to Alpine lamp radiation. The antibodies possessed most of the characteristics of reagins such as thermolability, exhaustibility, and affinity for skin. They differed from reagin, however, in that they lost their activity after a few weeks' storage in a liquid or lyophilized state. The fact that passive transfer of light sensitivity could be accomplished in all subjects suggested that "the antigen with which the antibody in the blood serum of this patient reacts is a substance which

normally is produced in the skin of all human beings upon exposure to sunlight or to Alpine lamp irradiation." No reaction occurred at the passively sensitized site when it was covered and the rest of the skin was irradiated with sunlight for several hours. This suggested that the urticariogenic antigen produced by light was not diffusible. There was some indication that histamine or a histamine-like substance was liberated after an attack of whealing produced by Alpine lamp irradiation, since a slight rise in the free and total gastric acidity occurred about twenty minutes after exposure. A.

A New Technique for Performing Quantitative Contact (Patch) Skin Tests. Dunn, J. E., Mason, H. S., and Smith, B. S.: J. Invest. Dermat. **6**: 323, 1945.

The authors describe a method for performing quantitative patch tests with sensitizing compounds which are soluble in volatile solvents such as acetone. With this technique the exact amount of test substance is known and, since it is applied with a volatile solvent, it is available for absorption as soon as it is placed on the skin. The test substance is uniformly distributed over a controlled area of the skin by the use of a brass ring barrier which is surrounded by a starch-glycerin sealing compound. It was found that the applied dose was about one-fifth less than the measured dose. A.

Penicillin Urticaria. Zeller, M.: Ann. Allergy **3**: 361, 1945.

In a patient receiving 25,000 Oxford units of penicillin every three hours, urticaria increased in intensity with each successive dose. Five days after the therapy was discontinued the skin was again normal. During the reactive phase as little as 50 units of commercial penicillin sodium produced urticaria, whereas during the week following the cessation of symptoms increasing doses of penicillin up to 25,000 units caused no reaction. During the reactive phase, commercial penicillin sodium elicited positive intracutaneous and passive transfer tests but a negative ophthalmic reaction. These positive reactions were, however only temporary since after the reactive phase they could no longer be elicited. H.

Percutaneous Photosensitization Due to Handling Parsnips. Starck, V.: Acta dermat.-venereol. **25**: 179, 1944.

An unusual type of occupational dermatitis of the hands was observed in thirteen patients who had been handling parsnips for several weeks. The dermatitis was found to be due to photosensitization following contact with parsnips. The photosensitivity persisted for several weeks after parsnip contact had been discontinued. Parsnip juice itself produced no perceptible irritation of the skin. H.

Dermatitis Venenata Following Use of Penicillin Ointment. Markson, L. S.: Arch. Dermat. & Syph. **52**: 384, 1945.

Dermatitis of the eyelids and face were observed within twenty-four hours following a single application of penicillin ointment to the eyes for the treatment of conjunctivitis. The patient had previously applied sulfathiazole ointment to the eyes for ten days without ill effects. Patch tests were performed with both sulfathiazole and penicillin ointment and were read twenty-four hours later. A positive reaction was observed with penicillin ointment. A.

Fixed Bullous Eruption Due to Sulfathiazole. McGuire, J. A., and Shaffer, B.: Arch. Dermat. & Syph. **52**: 342, 1945.

A fixed bullous eruption caused by sulfathiazole was observed in a patient under treatment for gonorrhea. The same type of eruption had occurred three months previously following the initial course of sulfathiazole. The lesions had occurred at precisely the same sites where the bullae were now present. Passive transfer studies were made with blister fluid from the sites of the fixed eruption. The blisters were raised with cantharides on normal skin and on the sites of the healed lesions. The passive transfer sites were injected with sulfathiazole solution or were patch-tested with 5 per cent sulfathiazole in an oil in water emulsion base. Positive reactions were observed only when sulfathiazole solution was injected into the sensitized sites. Both immediate and delayed reactions were noted. The controls, consisting of normal sites injected with sulfathiazole, showed some reactions but these were smaller than those seen in the passive transfer sites. At the end of forty-eight hours each sensitized site showed an indurated papule, while the control reactions had disappeared. Control studies made with blister fluid from normal skin areas were all negative. A.

Cheilitis From Local Use of Penicillin Solutions in Mouth. Goldman, L.: Arch. Dermat. & Syph. **53**: 133, 1946.

A solution of sodium penicillin in sodium chloride (500 units per cubic centimeter) was employed as a mouth rinse three times daily for a recurrent aphthous stomatitis. After two days, a vesicular cheilitis with edema of the lips developed. The patient had previously shown no intolerance for stable calcium penicillin ointment (500 units per gram) which had been applied heavily with cotton applicators, several times daily for a month, to each of the ulcerated areas in the mouth. Patch tests with the sodium penicillin solution which the patient had been using gave positive reactions. Negative reactions were obtained with the calcium penicillin ointment and three other brands of sodium penicillin solution. Contact tests made on the buccal mucosa were negative. When penicillin ointment was rubbed over the lips no reaction occurred, but, when sodium penicillin solution was applied, the lip edema appeared in twenty-four hours. In four other cases, no reactions occurred from the topical use of calcium penicillin ointment. A.

Urticaria Due to Trinitrotoluene. Preston, J. F., Jr., and Watkins, C. A.: Arch. Dermat. & Syph. **53**: 134, 1946.

A 25-year-old woman, employed in the production of trinitrotoluene, developed an itching vesicular eruption on her hands nine days after her first exposure to this chemical. In one week the dermatitis disappeared and failed to recur, although she continued at the same work. Several days later she developed coryza and a cough which was followed by a generalized urticaria. Sibilant and sonorous râles were heard throughout the chest, and the patient complained of dyspnea. Within five minutes after the application of a patch test with trinitrotoluene she complained of itching of the chin. An urticarial eruption started at this site and extended downward over the entire body. The reaction was controlled by epinephrine. A macular erythema was noted within ten minutes at the site of the trinitrotoluene patch test. When one drop of trinitrotoluene in acetone solution was dropped on the skin an urticarial eruption appeared on the chin within four minutes. The patient subsequently was removed from the trinitrotoluene area and remained free of urticaria. This is the

first time that the authors have observed urticaria directly attributable to trinitrotoluene. Whether or not the trinitrotoluene was responsible for the asthmatic symptoms could not be determined. A.

Localized Sensitivity to Crude Penicillin. Report of a Case. McGuire, J. A.: Arch. Dermat. & Syph. **53**: 31, 1946.

Crude penicillin in the form of a compress or in an ointment base was employed in the treatment of a dermatitis of the right hand. After several applications, it was noted that the dermatitis began to spread. Patch tests were performed with crude penicillin ointment, with the culture fluid in which the penicillin was grown, and with the ointment base. Positive patch test reactions were obtained on the right hand only with crude penicillin. Patch and scratch tests with purified penicillin were negative. Patch tests with crude penicillin applied to the opposite arm and hand which had not been treated were negative. It was concluded that the sensitivity to penicillin was localized to the treated area. Passive transfer studies were inconclusive. A.

Acetylcholine in the Treatment of Allergic Conditions. Giordano, A. F.: Semana méd. **52**: 138, 1945.

Patients with atopic eczema, neurodermatitis, urticaria, angioneurotic edema, and bronchial asthma were treated by the subcutaneous administration of increasing doses of a 0.001 Gm. solution of acetylcholine hydrochloride. The first dose was 0.025 or 0.05 cubic centimeter. The drug is potent, and one must proceed cautiously to avoid excessive parasympathetic excitation with the increasing doses. Injections were given daily or on alternate days depending on the reactions following each dose. In some cases histamine or specific desensitization was administered simultaneously with the acetylcholine. Early improvement was reported with this type of treatment. This communication is in the nature of a preliminary report. J. L. Cortes.

Otorhinology and Ophthalmology

An Apparatus for the Introduction of Penicillin Aerosol Into the Nasal Accessory Sinuses With a Case Report of a Patient With Chronic Sinusitus. Barach, A. L., Garthwaite, B., Soroka, M., and Anderson, F. F.: Ann. Int. Med. **24**: 97, 1946.

An apparatus is described which creates negative pressure in the nasal passages and sinuses and by partial evacuation of air from the sinuses allows replacement with penicillin aerosol. Calcium penicillin was better tolerated by the nasal and sinus membranes than the sodium salt. The dosage of penicillin in the therapy of chronic pansinusitus requires further investigation. A case of chronic sinusitus is reported in which marked improvement took place following a combination of orally administered penicillin together with intermittent negative pressure and penicillin aerosol inhalation. H.

Tissue Changes Produced in the Nasal Mucous Membrane of Normal Mice by Prolonged Local Administration of Some Solutions Containing Sulfonamide Compounds. Callomon, F. T.: Arch. Otolaryng. **43**: 31, 1946.

Carefully controlled histologic studies of the effects of various sulfonamide solutions on the nasal mucosa of mice were done, and microscopic comparisons of the affected nasal tissues with normal nasal tissues during and after prolonged administration were made. Tissue changes in varying degree were

found during treatment with all the sulfonamide solutions used, and return to normal in varying degree was observed in tissue specimens taken on the fifth day after the last treatment. There were marked differences of degree in the injury produced by the various solutions. When correlated with the pH values of the preparations used it was found that 3 per cent sulfathiazole in propylene glycol with a pH value near the normal physiologic range of nasal secretions in man showed the least irritating effect. Propylene glycol alone and isotonic sodium chloride alone showed no detrimental effect. The greatest injury and a slow return to normal was observed with a 2 per cent diasone solution in propylene glycol (pH 4.8). Solutions of succinylsulfapyrazine caused smaller inflammatory reactions than 3 per cent diasone, and cessation of treatment was followed by more rapid return to normal. A commercial preparation (desoxyephedrine and sodium sulfathiazole in aqueous solution of pH 9.2) caused an inflammatory and partly caustic effect during treatment and was followed by slow return to normal. A 2 per cent diasone solution (pH below 5) caused much greater damage than a 3 per cent alkaline solution of diasone with pH 8.8. C.

Intranasal Calcium Therapy in Allergic Rhinitis. Dimow, J.: Semana méd. **52**: 251, 1945.

After local anesthesia, a 10 per cent solution of calcium glucono-galactogluconate was injected into the submucosa at the base of both inferior nasal turbinates. The optimal quantity used was 2.5 c.c. of the solution.

The first four injections were given semiweekly, the next four were given weekly, and the next two were given biweekly. Hardening of the turbinates occurred without sclerosis. Sneezing, rhinorrhea, and itching were relieved in some cases after the first injection. The development of polypi was prevented. About 90 per cent improvement was obtained. J. L. Cortes.

Miscellaneous Allergies

Introduction of Allergens Into the Skin by Inunction With "Intraderm." I. Additional Experimental Data on the Inunction Test. Hermann, F.: Ann. Allergy **3**: 431, 1945.

Scratch and inunction skin tests were performed in sixty-seven cases of atopic dermatitis comprising seven hundred and seventy comparative sets of tests. "Intraderm" was the vehicle used for introduction of the allergen into the skin by inunction. The inunction test was positive in every case which reacted positively to the scratch test with the same allergen. In four instances, the inunction test was negative when a positive was obtained with the intracutaneous technique. Differences in reactivity were encountered in different skin areas with each of the methods. The skin surrounding the diseased areas gave stronger reactions than more distant sites. In some instances, in symmetrical normal skin areas, differences in intensity of reactions were found. Skin tests in the palm of the hand were consistently negative by the inunction method, weakly positive by the scratch method, and definitely positive by the intracutaneous method, although the response here was weaker than in other skin areas. J. Sherman.

Polyarteritis Nodosa: Report of 11 Cases With Review of Recent Literature. Logue, R. B., and Mullins, F.: Ann. Int. Med. **24**: 11, 1946.

Eleven patients with polyarteritis nodosa, ranging in age from 15 to 65 years, are reported. The duration of illness varied from two and one-half

months to one year. One patient recovered and was still well two years later. Hypertension was present in every patient at some time during the course of the disease. A personal history of allergy was absent in all eleven cases. None of the patients had received sulfonamide therapy. Leucocytosis was present in every case; eosinophilia (4 per cent plus) was noted in only five patients. Repeated examinations for eosinophilia should be made, as it is an inconstant finding and is probably related to periods of fresh activity. A review of the symptoms in one hundred and seventy-seven reported cases revealed the presence of eosinophilia in 33 per cent and a history of allergy in 21 per cent. It is suggested that the etiology of periarteritis nodosa is diverse and that perhaps it will be found that sensitization to serums, drugs, and infections may all play a part in the production of this disease. H.

Digestive Allergy: Sensitization to a Decomposition Product of Food Protein. Blamoutier, P.: Presse méd. **53**: 162, 1945.

The author reports a case of generalized urticaria and angioneurotic edema of ten years' duration, occurring five or six hours after the ingestion of lamb or mutton. Cutaneous tests with the raw allergens were negative. Cutaneous tests performed with the material obtained following incubation of the allergens with gastric or duodenal juice were also negative. Positive cutaneous and passive transfer tests were obtained with the material resulting from the simultaneous incubation of the allergens with both gastric and duodenal juices. This is offered as evidence that sensitivity may occur to a decomposition product of a food protein. Such sensitivities occur frequently in gastrointestinal allergy and food urticaria, in which cutaneous tests with whole allergens are negative. H.

A Study of One Hundred Cases With a Positive Coccidioidin Skin Test. Clark, D., and Gilmore, J. H.: Ann. Int. Med. **26**: 40, 1946.

In man, infection with *Coccidioides immitis* produces a sensitivity to coccidioidin which is similar to tuberculin hypersensitivity. A 1:100 dilution of coccidioidin without the addition of any preservative was used for cutaneous testing. One and eight-tenths per cent of the three hundred and seventy-two patients tested had equivocal reactions, characterized by an area of redness less than 0.5 cm. in diameter with little or no swelling. Subsequent testing on different skin areas resulted in positive reactions in some of these patients. One hundred and twenty-five of the three hundred and seventy-two patients tested showed positive coccidioidin reactions. No positive reactions were noted in individuals who had not been in areas endemic for Coccidioides. In no instance did the authors observe a cutaneous sensitivity develop following repeated testing. In two cases the cutaneous reaction became negative as the patients became desperately ill with a disseminated form of the disease. Complement fixation and precipitin antibodies for Coccidioides may be found in the blood, spinal fluid, and chest fluid in the active stages of the disease. The clinical picture and pathologic and roentgenographic findings in cases with Coccidioides infestation are fully discussed. H.

Transcutaneous Tuberculin Test (Cooper). Holden, L. W.: Am. Rev. Tuberc. **53**: 129, 1946.

A potent purified tuberculin was dried, powdered, and incorporated in a "nonirritating and nonallergizing transparent liquid preparation" which

adhered well to the skin. Tests performed by this technique were compared with the standard intracutaneous tests on groups of college freshmen. Variable results were obtained with the transcutaneous preparation possibly because of variation in the fineness of the powdered tuberculin, settling of the powder in the carrier, and evaporation of solvent from the preparation. The results of the transcutaneous tests were roughly comparable with those obtained with 0.0002 mg. of purified protein derivative administered intracutaneously. E. Kailin.

Observations on the Specificity and Clinical Use of Dirofilaria Immitis Antigen in the Diagnosis of Human Filariasis (Wuchereria Bancrofti). Zarrow, M., and Rifkin, H.: Am. J. M. Sc. **211**: 97, 1946.

An extract of *Dirofilaria immitis* was prepared. Persons infested with various parasites were tested intracutaneously with 0.05 c.c. of the extract. A positive reaction elicited with a 1:2,000 dilution of the original extract was regarded as a specific indication of filarial infestation. With this dilution no positive reactions were obtained in individuals known to harbor roundworms such as *Uncinaria americana, Strongyloides stercoralis, Ascaris lumbricoides,* and *Enterobius vermicularis.* Cross reactions were observed, however, when extracts of greater potency were used. Ninety-one per cent of patients having clinical filariasis showed a positive skin reaction to some dilution of the test antigen. A group of fifty-three persons exposed to filariasis was tested. Seventy-four per cent of this group showed a skin reaction to filaria extract. In 60 per cent of those having positive tests, biopsy proved the presence of filarial infestation. In some instances, several biopsies were done before the parasite was found. E. Kailin.

Studies on the Specificity of Intradermal Tests in the Diagnosis of Filariasis. Augustine, D. L., and Lherisson, C.: Am. J. Hyg. **43**: 38, 1946.

The diagnostic significance of positive intracutaneous reactions obtained with *Dirofilaria immitis* in suspected cases of Bancroftian filariasis is questioned. Positive reactions were noted in a large percentage of cases after extended residence in endemic areas, although no evidence of filarial infection was found in these cases. Many patients with acute symptoms regarded as characteristic of Bancroftian filariasis gave negative reactions. The present studies indicate that the false positive reactions may be due to sensitization resulting from repeated exposure to related nonhuman filarial worms (parasites in birds, etc.) the immune response being produced by the filarial larvae of such animals. H.

Thiouracil as a Cause of Neutropenia and Agranulocytosis. Lesses, M. F., and Gargil, S. L.: New England J. Med. **233**: 803, 1945.

Sixty-two patients, all but one of whom had thyrotoxicosis, were treated with thiouracil. Five patients developed agranulocytosis; of these, one died. These five cases are presented in detail. Two of them showed an eosinophilia up to 12 per cent during the period of recovery from the agranulocytosis. The literature on agranulocytosis caused by thiouracil is reviewed. The condition is thought to be the result either of depression of the bone marrow causing arrest of maturation of leucocytes at the promyelocyte stage, or of destruction of white cells beyond the promyelocyte stage. Size of the daily dose, duration of administration, and hypersensitivity to the drug are postulated as possible causes of this condition. Thiouracil is closely related chemically to barbital (diethyl barbituric acid) and may produce drug fever, urticaria, and other skin erup-

tions. Its readministration in small doses after a neutropenic reaction was not usually followed by recurrence of neutropenia. This was attributed to desensitization. J. Sherman.

Anaphylaxis

The Use of Papaverine Hydrochloride in the Prevention of Anaphylactic Shock in Guinea Pigs. Frank, D. Edward: J. Immunol. **52**: 59, 1946.

Papaverine hydrochloride in concentrations which protected 53 per cent of sensitive guinea pigs from fatal anaphylactic shock failed to prevent fatal histamine shock. It is suggested that the concentration of histamine in the shock organ is less in anaphylactic shock than that resulting from the experimental injection of histamine. Most of the surviving animals showed some symptoms of anaphylaxis suggesting that papaverine does not prevent the union of antigen and antibody but counteracts the action of histamine.
J. Sherman.

On the Thrombopenia of Anaphylactic and Peptone Shock. Quick, A. J., and Baronofsky, D. D.: Am. J. Physiol. **145**: 273, 1946.

Thrombopenia is a characteristic finding in both anaphylactic and peptone shock. Previous studies have shown that histamine bears no relation to this phenomenon. Clumping of the platelets occurs just prior to the thrombopenia. No correlation could be found between the severity of the shock reaction and the degree of thrombopenia. Marked thrombopenia was found to occur even when the shocking dose produced no apparent systemic reaction. Splenectomy had no effect on the occurrence of thrombopenia in peptone shock in dogs. The delay in coagulation time observed in shock was found to be the result of an outpouring of heparin into the circulation. The intravenous administration of large amounts of heparin did not, however, prevent the occurrence of platelet agglutination. The factors responsible for thrombopenia are, as yet, unknown.
H.

Observations on the Nature of the Antagonism of Histamine by 3-Dimethylaminoethyl Benzhydrl Ether (Benadryl). Wells, J. A., Morris, H. C., Bull, H. B., and Dragstedt, C. A.: J. Pharmacol. & Exper. Therap. **85**: 122, 1945.

The depressor effect of histamine was studied on anesthetized dogs before and after the intravenous injection of Benadryl. The antagonistic effect against histamine produced by Benadryl hydrochloride in doses of 3 mg. per kilogram persisted with little change for two hours. A constant percentage of the histamine acid phosphate administered intravenously was counteracted by a given dose of Benadryl, regardless of the dose of histamine given. When the dose of histamine was held constant and the dose of Benadryl increased, it was found that the degree of histamine inhibition rose sharply in the low dosage range. Dose increases beyond 1 mg. per kilogram, however, produced only slight increases in effect. Benadryl in a dose of 0.1 mg. per kilogram antagonized 55 per cent of the injected histamine, 0.2 mg. doses counteracted 68.5 per cent, 1 mg. doses counteracted 85.2 per cent, 4 mg. doses counteracted 93.8 per cent, and 16 mg. doses counteracted 97.1 per cent. When these values are plotted, a rectangular hyperbole is obtained, a curve which almost exactly follows the formula for the Langmuir isotherm adsorption equation. The authors concluded that Benadryl is adsorbed at the site of action of histamine so that "a given amount of histamine has much less opportunity to reach and combine with its site of action." E. Kailin.

Effect of Various Drugs on Experimental Asthma Produced in Guinea Pigs by Exposure to Atomized Histamine. Loew, E. R., Kaiser, M. E., and Moore, V.: J. Pharmacol. & Exper. Therap. **86**: 1, 1946.

When histamine is atomized in a cubicle under controlled conditions, from 75 to 100 per cent of the guinea pigs in the enclosure die in acute asphyxia. When the animals are injected intraperitoneally with aminophylline in doses of 50 mg. per kilogram prior to exposure to histamine, the mortality rate is reduced. The protective effects of other drugs were rated on the basis of the ratio between their minimal effective doses in terms of weight per kilogram of guinea pig and the 50 mg. per kilogram dose ("activity index of unity") of aminophylline. Papaverine, in doses of 25 mg. per kilogram, was accorded an activity index of 2. Other activity indices were as follows: atropine, 3; Demerol, 8; Benadryl, 33; and epinephrine, 500. However, large doses of epinephrine failed to reduce mortality to zero, but large doses of Benadryl did have this effect. Ephedrine *increased* the mortality rate. Pentobarbital and morphine failed to lower the mortality rate. Caffeine, Trasentin, Pavatrine, Syntropan, Tuamine sulfate, ergotamine tartrate, Procaine, and Nupercaine were ineffective. Physostigmine aggravated the histamine shock. E. Kailin.

The Anti-Histamine Action of Alkyloxytriazines and Related Compounds. Loew, E. R., Kaiser, M. E., and Anderson, M.: J. Pharmacol. & Exper. Therap. **86**: 7, 1946.

Five alkyloxytriazines were found to be four times as effective as aminophylline in reducing the mortality of guinea pigs subjected to atomized histamine. Three of these compounds were effective when given orally. Similar compounds which lacked an ether linkage in the side chain were ineffective even when administered parenterally. The toxicity of the effective chemicals in mice was about one-half that of aminophylline. These animals exhibited ataxia, vasodilatation, depression, and hypnosis. In rabbits these compounds caused peripheral vasodilatation but no depression.

The antispasmodic action of three alkyloxytriazines was tested on segments of ileum suspended in a tyrode bath and contracted by histamine, barium chloride, or acetylcholine. Aminophylline counteracted the spasm produced by all of these agents equally well. The alkyloxytriazines were two to ten times as effective as aminophylline in counteracting the effect of histamine. One of these compounds was relatively ineffective in counteracting spasm induced by acetylcholine or barium. No such preferential action was exhibited by the other two alkyloxytriazines, indicating that their antihistaminic effect was not specific. E. Kailin.

Influence of Epinephrine and Atropine on the Pulmonary Pressor Action of Histamine. Woodbury, R. A.: J. Pharmacol. & Exper. Therap. **83**: 79, 1946.

Histamine usually produces a rise in pulmonary arterial tension in cats. Direct blood pressure recordings of the pulmonary artery, pulmonary vein, and carotid artery in anesthetized cats showed that epinephrine inhibited the systemic fall in blood pressure elicited by histamine but did not significantly reduce the high pulmonary tension and greatly increased pulmonary pulse pressure. Large doses of atropine failed to counteract either the systemic depressor or the pulmonary pressor effects of histamine but delayed the appearance of the pulmonary pressure rise. This is in contrast to the inhibitory effect of atropine on isolated histamine-contracted pulmonary arteries of the rabbit.

E. Kailin.

Miscellaneous

Decreased Antigenicity of Coupled Hapten-Protein Antigen Resulting From Treatment With Too Much Hapten. Boyd, W. C., and Warshaver, E. R.: J. Immunol. **52**: 97, 1946.

Aromatic amines (haptens) may be coupled with protein by means of a diazo linkage. It is generally believed that the diazonium compound couples with the protein through the tyrosine and histidine residues. It has been previously shown that when coupled hapten-protein antigens are treated with too much hapten the antigenicity of the compound is decreased. Rabbits were injected with horse serum which was diazotized with six times the amount of arsanilic acid which would theoretically be sufficient to saturate the histidine and tyrosine. Four different arsanilic proteins prepared in the same manner were injected into thirty rabbits and bleedings were taken at frequent intervals. Only faint traces of antiarsanilic antibody were found in the sera, none of which flocculated with the test antigen. Rabbits injected with proteins diazotized with amounts of arsanilic acid just sufficient to combine with the histidine and tyrosine of the protein usually produced sera strong enough to flocculate with test antigen. Some had previously failed to produce antibodies when injected with the supersaturated antigen. It was also apparent that animals injected with the antigen that contained too much hapten failed to produce as much antibody against the protein carrier (horse serum) as did those animals injected with antigen with less hapten. It was concluded that when coupled hapten-protein antigen is treated with too much hapten its antigenicity is decreased. A.

Criteria of Eosinophilia. Discombe, G.: Lancet **1**: 195, 1946.

The various methods used for accurate hemocytometer eosinophile counts are reviewed and a new technique is proposed. One part of blood is diluted with twenty parts of staining fluid, five volumes each of 1 per cent aqueous eosin Y and of acetone and 90 volumes of distilled water. The pipette is then shaken vigorously, the Fuchs-Rosenthal chamber is filled, and the count is made. The normal eosinophile count is 0 to 240 cells per cubic millimeter. A mild eosinophilia of 400 to 500 cells per cubic millimeter was demonstrated in most quiescent asthmatics. This technique is recommended as an accurate, rapid technique for eosinophile studies. H.

Immunity Response of Mothers and Babies to Injections of Pertussis Vaccine During Pregnancy. Hendrich, P., Thompson, M., and Eldering, G.: Am. J. Dis. Child. **70**: 25, 1945.

The authors studied ninety-nine pregnant women of whom fifty-seven were immunized with pertussis vaccine. The opsonocytophagic reaction was used as a measure of circulating antibodies. The women were tested before parturition and again, with their babies, soon after delivery. Immunization was completed one month before parturition and was followed by a pronounced rise in titer in 80 per cent of the group. In general, the titers for the babies varied with those of their mothers but were at a lower level. In the immunized group, the ratio of the baby's titer to that of the mother was 1:1.5, and in the nonimmunized group, the ratio of baby to mother was 1:2.2. The ratio of titers of immunized to nonimmunized mothers was 1:2, and that of their babies 1:2.9. Hence, placental transfer of pertussis circulating antibodies does occur. The higher the titer in the mother, the more closely does the titer of the baby approach her own. E. Walzer.

Allergy Abstracts

Asthma and Hay Fever

Penicillin in the Treatment of Bronchiectasis. Bobrowitz, I. D., Eldin, J. S., Bassin, M. D., and Wooley, J. S.: New England J. Med. **234**: 141, 1946.

Twelve patients ranging in age from 16 to 30 years and suffering from severe bronchiectasis were treated with large doses of penicillin over long periods of time. The total dosage of penicillin administered varied from 550,000 to more than 5,500,000 Oxford units, and treatment was continued for from four to one hundred fifteen days. The doses were given intramuscularly, intratracheally, or by inhalation. The highest concentration of penicillin in the sputum was attained by intratracheal instillation, and the results were obtained most quickly by this route. Inhalation proved less effective and intramuscular injection least effective. Excellent results were obtained with penicillin therapy. The amount of sputum was diminished, the odor was eliminated, and the amount of purulent material was sharply reduced. Most of the organisms were eliminated. The remarkable improvement continued only so long as penicillin was administered and the authors surmise that penicillin therapy would have to be continued indefinitely in these cases. Penicillin therapy is recommended for symptomatic relief in nonoperative cases of bronchiectasis and as preoperative preparatory treatment for lung resection for bronchiectasis.

Asthma as Observed Overseas in a General Hospital in the Southwest Pacific Area—With Special Reference to Relationship of Tropical Service to Onset and Recurrence. Winkenwerder, W. L.: Bull. Johns Hopkins Hosp. **78**: 78, 1946.

Of the total admissions to a general hospital in the Southwest Pacific Area, 1 to 2 per cent of the patients had bronchial asthma. Two hundred nine of these were studied in detail. Most of the asthmatics gave a past personal or family history of allergy or showed positive skin tests. Sixty-four per cent of the one hundred two patients who developed asthma after entry into the Army had their first episode in the tropics, 16 per cent in Australia and 20 per cent in the United States. In the tropics, hay fever symptoms accompanied the asthmatic attacks in about one-half of the patients. The incidence of symptoms was perennial. Many patients developed symptoms within two weeks following their arrival in the tropics and the majority had trouble within three months. Specific etiological factors were grass pollen, algeroba tree pollen, mold spores, and tropical dust, which has about twenty times the protein nitrogen content of dust in the United states. Other contributing factors were excessive humidity, wide daily temperature variation, and strong aroma of molds, and strenuous military life. The average disability period approximated two months per man, and 82 per cent of the group had to be evacuated to the United States. E. KAILIN.

Bronchial Asthma and Lumbar Puncture. Jonuleit, R.: Ztschr. f. klin. Med. **142**: 292, 1943.

Lumbar puncture and the removal of a few milliliters of spinal fluid resulted in general improvement in a series of eight patients with severe bronchial asthma. No improvement was noted in one patient with cardiac decompensation. The

vital capacity was increased after lumbar puncture. This form of treatment in bronchial asthma was first introduced in 1919 and rediscovered in 1939. The mechanism by which this procedure works is unknown. Reflex effects on the vegetative centers of the brain have been suggested as an explanation. H.

The Prognosis for Bronchial Asthma Arisen in Infancy After the Nonspecific Treatment Hitherto Applied. (An Investigation in the Fate of 298 Asthmatic Children.) Flensborg, E. Winge: Acta. pediat. **33**: 4, 1945.

A questionnaire was sent out to three hundred thirty-eight children hospitalized for bronchial asthma from 1926 to 1939. Two hundred ninety-eight replies were reviewed. This group included 63 per cent males and 37 per cent females. In 66.4 per cent, the onset of bronchial asthma had occurred before the age of 5, mostly in the second and third years. In twenty patients asthma started during the first year, and nineteen of these continued to have asthmatic attacks. If bronchitis were to be accepted as the criterion of the onset of the asthma, the average age of onset would be considerably earlier. Among those who replied, attacks of asthma had ceased in 40 per cent and had been recurrent in 54 per cent. Five per cent (15) had died, one-third of them in status asthmaticus. Of one hundred thirty-one, who reached the age of 18 years, 41 per cent had no asthma. Of one hundred sixty-six reaching 20 years of age, 46 per cent had no asthma. Environmental change was the most important factor in clearing the asthma. Forty-four per cent of those who had no asthma still had some dyspnea on exertion. H.

Dermatology

Inhibition of Experimental Drug Allergy by Prior Feeding of the Sensitizing Agent. Chase, M. W.: Proc. Soc. Exper. Biol. & Med. **61**: 257, 1946.

Guinea pigs were fed 0.3 ml. of a 1 per cent solution of 2:4 dinitrochlorobenzene in olive oil daily for six days followed by an eight-day rest period. Two or three such courses were given prior to an attempt at sensitization by intracutaneous injections. While the latter technique regularly sensitized normal animals, or animals fed the vehicle alone, a considerable diminution in effect was encountered in groups that had received prior feeding of the chemical. These "resistant" animals when injected with a nonrelated chemical were readily sensitized to the new agent. Similarly, animals, which were fed one chemical and then sensitized simultaneously with this and another allergen, showed blocking only for the antigen which had been ingested. The blocking mechanism was found to persist as long as twenty-seven weeks after the final ingestion of the antigen. Hence, the feeding of certain allergenic compounds to nonsensitive animals induces a state of resistance against subsequent experimental skin sensitization by the same substance. E. WALZER.

Studies in Hypersensitivity to Light. II. Urticaria Solare ($\lambda <$ 3700). Blum, H. F., Baer, R. L., and Sulzberger, M. B.: J. Invest. Dermat. **7**: 99, 1946.

Further studies were conducted on a case of photosensitivity manifested by urticaria covering the area of the skin exposed to light. Wave length studies were made with a special apparatus in an effort to clarify the etiology of the condition. The source of radiation was an intermediate pressure mercury arc of known spectral emission and the dosage was controlled by means of a photocell and other devices which measured the ultraviolet radiant energy delivered. The

lowest effective dose which produced only a trace of erythema was regarded as the threshold dose. Various types of spectral filters were employed, and it was determined that the sensitivity of the patient's skin was most pronounced to wave lengths from 3130A to 3650A and failed to respond beyond the latter wave length. The limit of the patient's sensitivity was, therefore, placed at approximately 3700A which lies entirely in the ultraviolet zone. It was also found that the patient was highly sensitive to the wave lengths which produce sunburn on normal skins and that his sensitivity extended to longer wave lengths. Although sunburn-producing radiation comprises only a small fraction of maximal summer sunlight and is usually absent during the winter, the urticarial response in this case was elicited by a much larger fraction of sunlight and even during the winter short exposures produced a skin reaction. Whereas a normal individual is completely protected from sunburn if the light is filtered through ordinary window glass, this patient was not protected. Urticaria in this patient could be elicited by doses about two orders of magnitude less than those which produce sunburn. Wheals could be produced on normal skin sites sensitized with the patient's blood serum by exposing them to the same wave lengths which elicited urticarial responses on the patient's skin. The possibility that the light absorber is an antibody must be considered, since the light absorber in the skin and in the serum on passive transfer appear to be identical. However, unconjugated proteins are known to absorb radiation although they absorb relatively little of the longer wave lengths between 3200A and 3700A to which this patient is sensitive. A.

Reactions to Penicillin Therapy. Kolodny, M. H., and Denhoff, E.: J. A. M. A. **130**: 1058, 1946.

Among one hundred twenty-four young male patients treated intramuscularly with penicillin sodium, twenty-one developed immediate reactions. Of these, eighteen occurred among dermatologic patients and in all but one there were exacerbations of the pre-existing skin lesions with pruritus, hyperemia, and exudation. All of the reactions had their onset ten to twenty-four hours after the beginning of treatment and all but three subsided within three to four days. In four patients, an "id-like" reaction of the hands and feet occurred. None of the immediate reactions were of an urticarial or febrile type.

Delayed reactions occurred in eleven of the one hundred twenty-four patients, with an even distribution among the dermatologic and nondermatologic cases. With one exception (twenty-three days), they occurred from seven to fourteen days after the beginning of treatment. The reactions varied in severity and were always urticarial and pruritic. Five of the patients also developed arthralgia, edema of the face, lymphadenopathy, myalgia, and malaise. Almost all subsided in four to five days.

The incidence of immediate and delayed reactions to penicillin bore no apparent relationship to previous penicillin treatment, either local or parenteral. A large number of patients who had had reactions were able to take subsequent courses of penicillin without difficulty. A few consistently reacted to penicillin but only when an interval of more than one week elapsed between courses. This seemed to indicate that a temporary anergic state exists for several days after a reaction. Skin tests with 0.1 c.c. of penicillin and trichophytin were performed on fifteeen reactors and fourteen nonreactors. Of the fifteen reactors eleven gave positive skin tests to penicillin and nine to trichophytin. Eight of the latter group were also positive to penicillin. Only two of the nonreactors gave positive tests to penicillin while five of this group were positive to trichophytin. Hence, fungus infections seem to play an important role in the production of these reactions to penicillin. F.

Urticaria Solare (λ 4000A-5000A). Blum, H. F., Barksdale, E. E., and Green, H. G.: J. Invest. Dermat. **7**: 109, 1946.

Urticaria solare was observed in a 19-year-old white man who gave a history of having been stung by an insect just prior to the onset of his photosensitivity. Twelve areas of the back were exposed to sunlight through various glass filters of known spectral transmissions. The urticarial response occurred only under those filters which transmitted radiation within approximate wave lengths of 4000A to 5000A. These wave lengths represent the blue and violet portions of the visible spectrum and elicit no specific response from normal skin. Urticaria produced by these wave lengths appears to be a distinct clinical entity. Passive transfer of this sensitivity could not be accomplished. Spectroscopic examination of the skin and blood serum failed to detect the presence of excessive amounts of carotinoid pigments which might specifically absorb wave lengths between 4000A and 5000A. Limiting the oxygen supply by cutting off the circulation to the arm with a sphygmomanometer cuff did not prevent the development of urticaria on the exposed part. Treatment with Hapamine parenterally failed to alter the photosensitivity. The exposed parts of the body such as the face and hands were less sensitive to light than the parts usually covered by clothing. Window glass failed to protect this patient against the reaction from sunlight, and exposure to fluorescent lighting produced a reaction of the skin. A.

Theophylline Ethylenediamine as an Antipruritic Agent. Epstein, E.: Arch. Dermat. & Syph. **53**: 281, 1946.

Theophylline ethylenediamine when injected intravenously in a dose of 0.5 Gm. in 20 c.c. of fluid produces immediate relief in patients with generalized or localized itching. Twenty-five patients suffering with various types of itching dermatoses, including poison oak and other forms of contact dermatitis, disseminated neurodermatitis, exfoliative dermatitis, and localized eczema of the hands experienced immediate relief of itching following one or more intravenous doses of theophylline ethylenediamine. The relief lasted from thirty minutes to twelve hours, the average being four hours. When itching recurred, it was usually less severe than previously. Once the itching was relieved, the lesions usually responded more rapidly to local treatment. The injection was never repeated more than once in a twenty-four-hour period. The mechanism by which this drug produces relief of pruritus has not been determined. The dangers of the promiscuous intravenous use of theophylline ethylenediamine, particularly in patients with impaired cardiac reserve, are stressed. The toxicity of the drug is decreased when 0.5 Gm. is administered in 1,000 c.c. of 5 or 10 per cent glucose, but the relief of itching is not as effective with this solution. Beneficial effects have been observed, however, when the drug is injected intramuscularly in doses of 0.5 Gm. in 2 c.c. of fluid. A.

Lemon Grass Oil (Primary Irritant and Sensitizing Agent). Mendelsohn, H. V.: Arch. Dermat. & Syph. **53**: 94, 1946.

Lemon grass oil contains approximately 70 to 80 per cent of citral, a diolefinic aldehyde, and a common constituent of essential oils. From lemon grass oil, it is possible to isolate three different ionones, which represent the aldehyde citral converted to a ketone. Iones are highly aromatic and are used in cosmetics. A group of twenty patients suffering with acne, dermatitis venenata, dermatophytosis, eczema, folliculitis, impetigo, etc., were patch tested with three lemon grass oils and the three ionones. The lemon grass oils were employed undiluted and in dilutions of 1:10 and 1:100 in olive oil. Patch tests were read in twenty-four to forty-eight hours. Undiluted lemon grass oil with a

citral content of 75 per cent or over was found to be a primary irritant and produced positive contact reactions in every person tested. A high incidence of positive contact reactions was also obtained with lemon grass oil diluted 1:10. In one patient, delayed reactions were observed to all oils in a 1:10 dilution on the sixth day, suggesting induced sensitivity or spontaneous flare-up reactions. When the same patient was retested three weeks later, reactions were observed within forty-eight hours. This finding was considered evidence of the sensitizing qualities of lemon grass oil. Patch tests performed with the three ionones were negative in all cases, indicating that ionones are neither irritating nor sensitizing. A.

Treatment of Hypersensitiveness to Cold With Benadryl. Report of a Case. Notier, V. A., and Roth, G. M.: Proc. Staff Meet., Mayo Clin. **21**: 170, 1946.

A white woman, aged 44 years, gave a history of hypersensitivity to cold since the age of 6 years. Exposure to cold air caused tingling, itching, burning, erythema, and swelling of the skin of the face, arms and legs. Dyspnea, nasal congestion, lacrimation and rhinorrhea occurred when she breathed cold air. The personal and family history were negative for allergy. There was a history of duodenal ulcer since she was 18 years of age. Immerson of the hand in ice water at 10° C. for five minutes produced pallor of the skin of the hand, burning and tingling of the immersed portion of the arm, and marked swelling of the arm within ten minutes after exposure. When the test was repeated at the end of eighteen days, during which time the patient had been receiving four doses of 50 mg. of Benadryl daily, more than 50 per cent improvement was noted. Because of gastric distress following the ingestion of Benadryl, the number of doses was reduced to two daily, for the next month. At the end of this period, the drug was discontinued and the improvement began to decrease. It is suggested that Benadryl does not appear to be a particularly effective therapeutic measure for cold hypersensitiveness, especially in the presence of a duodenal ulcer. A.

Allergy to Penicillin Calcium Topically in Blepharoconjunctivitis. Benkwith, K. B.: U. S. Nav. M. Bull. **46**: 279, 1946.

A severe allergic reaction occurred following the instillation of drops of penicillin calcium solution into the lower conjunctival cul-de-sac for the treatment of a purulent blepharoconjunctivitis. The patient had been receiving 6 drops of penicillin hourly for two days when the reaction developed. The lesions consisted of edema, redness, and weeping of the skin of the lids, nose, and malar region and were accompanied by intense itching. An intracutaneous test with calcium penicillin solution resulted in an urticarial reaction in twenty-four hours. A patch test with penicillin ointment was markedly positive. Control tests were negative. The lesions disappeared following cessation of penicillin therapy. A.

Procaine Intravenously in Treatment of Delayed Serum Sickness. State, D., and Wangensteen, O. H.: J. A. M. A. **130**: 990, 1946.

Severe myalgia, arthralgia, and other symptoms of serum reactions were promptly relieved by the intravenous administration of procaine. Along with the relief of pain, subsidence of all the manifestations of serum sickness occurred in a large percentage of the patients treated. The procaine was given in doses of 1 Gm. in 500 c.c. of saline over a period of two hours. In a total of twenty-seven patients treated, there were no untoward reactions. Of fifteen patients who had developed serum sickness following the injections of crystalline bovine albumin solution, ten obtained complete relief, four had temporary re-

lief, while two were not benefited. In one case of serum sickness which followed the administration of antitetanus serum the results were striking. Six of seven patients with urticaria obtained various degrees of relief. One patient with chronic asthma and another with chronic deforming rheumatoid arthritis were not benefited. The mode of action of procaine is not known but the authors suggest that it may be by (1) direct action on the cells, (2) an antihistamine action, (3) antiacetylcholine action, or (4) an epinephrine potentiating action of procaine. F.

Otorhinology and Ophthalmology

Experimental Histological Studies on the Labyrinth. VI. Anaphylaxis. Mygind, J. H., and Andersen, H. C.: Acta Oto-laryng. **33**: 406, 1945.

Histologic studies were done on the nasal mucosae and labyrinths of shocked guinea pigs. In one group (A), inverse anaphylactic shock was produced by the intracranial injection of 1.5 c.c. of Forssman antibody, titer 20,000. All the guinea pigs died in convulsions, but without noticeable vestibular or nasal reactions. Microscopic examination of the nasal mucosae showed only hyperemia. In another group (B), violent clinical nasal reactions followed the intranasal instillation of Forssman antibody, titer 20,000. Histologically, the nasal mucosae showed pronounced subepithelial serous exudation, hyperemia, eosinophilia, and secondary epithelial changes. There were no vestibular symptoms. A third group (C), sensitized and shocked with antigen from the urine of pregnant women, showed marked hyperemia, edema, and serous exudation of the nasal mucosae but no vestibular symptoms. Histologic changes in the labyrinths consisted of slight compression of Reissner's membrane in Group A, marked compression in Groups B and C, and compression of the organ of Corti in Groups B and C. C.

Post-Nasal Drip: The Current American Nightmare. Proetz, A. W.: Ann. Otol., Rhin. & Laryng. **54**: 739, 1945.

Certain abnormal states cause the mucus of the nasopharynx to become excessive, abnormally viscous, abnormally fluid, mechanically or chemically irritating, odorous, or obstructive. Among the causes which may produce these abnormal changes are central heating systems; the excessive use of tobacco or alcohol; thermal changes; local mechanical abnormalities; malignant and nonmalignant lesions; dusts; fumes; bacteria; viruses; fungi; allergens (inhaled or ingested); atrophy; foreign bodies; metabolic, endocrine, or emotional disturbances; and excessive and prolonged medication. Each of these factors is discussed from the point of view of mechanism and relative importance. Postnasal drip is frequently the result of modern living conditions some of which are irremediable and may be harmless. The postnasal discharge is often a physiologic response of the mucous membranes to an irritant which it helps to mitigate or remove. Treatment of the sinuses in such cases will often fail because the cause lies elsewhere. C.

The Roentgen Treatment of Vasomotor Rhinitis. Renander, O.: Acta. Otolaryng. **33**: 44, 1945.

Roentgen therapy for allergic nasal conditions has been in use since 1915 when it was first successfully applied to hay fever. The author has treated two hundred twenty-six cases of vasomotor rhinitis, mostly in young adults. Forty-two per cent of the cases were complicated by sinusitis, 19 per cent by asthma,

and 10 per cent by both sinusitis and asthma. Freedom from nasal symptoms resulted in 67 per cent, improvement in 23 per cent, and in 10 per cent there was no change. Cases complicated by sinusitis and asthma did as well as uncomplicated cases. The duration of relief was more than one year in 50 per cent and more than two years in 41 per cent. The treatment consisted of three exposures over the nose and sinuses, at one- or two-day intervals, 100 to 150 roentgen units being the minimum effective dose. H.

Miscellaneous Allergies

Influence of Dimethylaminoethylbenzyhydryl Ether Hydrochloride Upon Histamine Flare Reactions. Elias, H., and McGavack, H.: Proc. Soc. Exper. Biol. & Med. **61**: 133, 1946.

β-Dimethylaminoethylbenzyhydryl ether hydrochloride (Benadryl), when orally administered in sufficient amounts, is capable of suppressing the reaction of the skin to histamine. Nonallergic patients who had no recognizable disturbances of the autonomous nervous system were subjected to histamine skin tests before, during, and after oral administration of varying amounts of the drug. A diminution in both wheal and erythema was observed after three days' treatment with 150 mg. daily, and a complete disappearance occurred in some cases after ten days' treatment with 300 mg. daily. Upon discontinuing the drug, the response to histamine in every case became accentuated as compared to the control. In one case, the flare and wheal became 500 per cent greater than at the start. The reaction usually returned to normal within a few days after the drug was stopped. It is suggested that its antihistamine action accounts for the clinical value of the drug. J. SHERMAN.

The Inunction of Allergens With "Intraderm." II. Desensitization by Allergen Inunctions. Hermann, F.: Ann. Allergy **4**: 4, 1946.

Desensitization by inunction of allergens into the skin with "Intraderm" was studied in twenty-two patients using fifty-four allergens. Allergen suspensions in "Intraderm" were provided for daily home applications. A reduction of skin reactivity resulted in most cases after varying periods of application. Both inunction and scratch tests became negative to 33 per cent of the allergens used; scratch tests alone became negative to 18 per cent of the allergens. Less than 4 per cent of the allergens failed to show reduction of reactivity. The inunction test appeared to be more sensitive than the scratch test. During the early phase of the inunction treatment, five patients showed transitory lesions, resembling atopic dermatitis, at the site of inunction. Fifteen of the twenty-two patients showed clinical improvement during the treatments. J. SHERMAN.

Sudden Death Following Intravenous Injections of Thiamine Hydrochloride. Reingold, I. M., and Webb, F. R.: J. A. M. A. **130**: 491, 1946.

The author reports the case of a 25-year-old woman who had received three large intravenous doses of thiamine hydrochloride without any serious reaction. A fourth dose of the same strength was followed within ten minutes by a generalized burning sensation, profuse perspiration, dyspnea, cyanosis, and death. Autopsy revealed constriction of the pulmonary arteries with pulmonary engorgement, right-sided dilatation and failure, and mild emphysema. This reaction was regarded as an allergic one, the patient having received three sensitizing injections previous to the fatal reaction. It was not considered likely that chlorobutanol could have caused the reaction. F.

Densensitization to Insect Bites. Hatoff, A.: J. A. M. A. **130**: 850, 1946.

One hundred twenty-nine infants and children susceptible to flea bites were treated with a polyvalent flea extract. Approximately 80 per cent of the group were benefited after an average of four subcutaneous injections of the antigen. The authors believe that this method of treatment may be used as an adjunct in the control of insect-borne diseases. F.

Toxic Reactions Accompanying Second Courses of Sulfonamides in Patients Developing Toxic Reactions During a Previous Course. Dowling, H. F., Hirsh, H. L., and Lepper, M. H.: Ann. Int. Med. **24**: 629, 1946.

Seventy-eight adult patients who developed fever, dermatitis, or conjunctivitis during the first course of sulfonamide therapy were observed during a second course of treatment. Thirty-three (69 per cent) of those who received the same sulfonamide during both courses developed one of the afore-mentioned symptoms. Only five (17 per cent) of those receiving a different sulfonamide during the second course of treatment developed a reaction. Neither the number of reactions during the first course nor the interval between the two courses had any effect upon the appearance of symptoms during the second course of treatment. The authors conclude that the incidence of reactions is less when a different sulfonamide is used for a second course of treatment, regardless of whether a reaction occurred during the first course. These findings confirm the generally accepted opinion that, in most instances, sensitivity to the sulfonamides is relatively specific for the individual drug, but that in some cases a group sensitivity develops which includes several or all of the sulfonamide drugs. H.

Transient Successive Pulmonary Infiltration (Loeffler's Syndrome). Eichwald, M., and Singletary, W. V.: Radiology **46**: 258, 1946.

A 49-year-old woman, admitted to the hospital for a minor gynecological disorder, was found to have a 21 per cent eosinophilia and a linear pulmonary shadow which was interpreted as thickened pleura. A cervical polypectomy was followed by uneventful convalescence. Two weeks later, the patient was again admitted to the hospital with vague complaints and a slight fever. Roentgenogram of the lungs showed a rather extensive irregular, bilateral mottling. Eosinophilia ranged as high as 29 per cent. Serial x-ray studies showed a frequently changing pulmonary picture. The condition failed to respond to sulfadiazine or penicillin. The patient's symptoms were always of a mild character. A parasitic etiology was ruled out. It was thought the process was the result of sensitivity to bacteria, possibly from the chronic cervicitis and endometritis. The lesion was considered as a secondary allergic response of sensitized tissue comparable to the "id" reaction and was therefore termed a "pneumonid." F.

The Relation of the Degree of Sensitivity to Tuberculin to the Persistence of Sensitivity and Prognosis in Young Children. Edwards, L. B., and Hardy, J. B.: Bull. Johns Hopkins Hosp. **78**: 13, 1946.

Children under 3 years of age were classified according to their maximum skin reaction to various dilutions of Old Tuberculin. Three groups were followed for an average of nine, five, and seven years, respectively. Group I comprised thirty-four children who showed a positive skin reaction to a dose of 1 mg. of Old Tuberculin. On retesting a year or more later, thirty of these children failed to react even to this dose and none developed any roentgenologic or other

evidence of tuberculosis. Group II included twenty-six children who showed a positive skin reaction to 0.1 mg. O. T. Eleven of this group became temporarily, and six permanently, skin test negative to this dose. Three children of Group II showed intrathoracic calcification, one had a parenchymal lesion of tuberculosis and two had extrapulmonary tuberculosis. None of Group II died. One hundred forty-seven children of Group III gave either vesiculated reactions to 0.1 mg. or a reaction of 0.01 mg. O. T. Of one hundred two patients retested, ten failed to react to the 0.1 mg. dose. Only seventeen children of this entire group failed to show some tuberculous lesion and twenty-two died of tuberculosis. E. KAILIN.

Fundamental Information on Mechanism of Specific Tuberculo-Immunity. Corper, H. J.: J. Lab. & Clin. Med. **31**: 346, 1946.

There are two distinct types of tuberculo-allergy, tuberculin sensitivity and allergy elicited by either viable or heat-killed tubercle bacilli. This latter type of allergy persists for less than one year. Tuberculin, a product of the autolysis of tubercle bacilli, appears in cultures only when the colonies are aging, and is probably not liberated in vivo. Tuberculin can induce anaphylactic sensitivity in animals and the anaphylactic sensitivity in animals and the anaphylactic antibodies, unlike either the immune or bacillary allergic principles, are passively transferable and can sensitize the fetus in utero. Animals anaphylactically sensitive to tuberculin cannot be shocked with young, washed tubercle bacilli. Bacillary-sensitized animals, however, and infected animals do exhibit anaphylactic shock when tubercle bacilli are injected. Desensitization to tuberculin anaphylactic sensitivity does not occur when the animal is infected with tuberculosis. Cutaneous sensitivity to tuberculin can be brought about only by the presence of the whole tubercle bacillus and does not appear in animals sensitized only with tuberculin. Active tuberculosis and allergic bacillary hypersensitivity are not affected by tuberculin immunization and tuberculin therapy for this purpose is not warranted. Infected bacillary-sensitized animals may die of marked tuberculous involvement but not of anaphylactic shock, when tuberculin is used in an attempt to bring on anaphylaxis.

Allergy and immunity to the tubercle bacillus are separate entities and may coexist in the same animal. Immunity is measurable only through the induction of a virulent infection. The available data point to the existence of a specific tuberculo-immunity which persists for more than four years and is brought about only by viable avirulent bacilli and not by nonviable bacilli, tuberculins, or the filtrate from bacilli. A case is presented of a patient infected with only avirulent tubercle bacilli, which do not increase their numbers in even a highly susceptible host. This man suffered a protracted fatal illness as a result of allergy to the bacillus. At autopsy his lungs showed fibrocavernous tuberculosis with a marginal acute hyperemia in the left lung. E. KAILIN.

Anaphylaxis

The Effects of Immunization With Histamine Azoprotein on Histamine- Intoxication and Passive Anaphylaxis in the Guinea Pig. Coffin, G. S., and Kabat, E. A.: J. Immunol. **52**: 201, 1946.

The protective action of immunization with histamine azoprotein against histamine intoxication and against passive anaphylaxis was studied in guinea pigs. One group of animals was treated with alum-precipitated histamine azoprotein and a second group with histamine azoprotein and adjuvants. A third group served as a control. When the minimal lethal dose of histamine was in-

jected intravenously, six of seven animals treated with alum-precipitate and nine of twelve treated with azoprotein and adjuvants died within five minutes. In the passive anaphylaxis experiments three groups of animals were prepared as described previously, a fourth was treated with human serum and adjuvants, and a fifth was treated with saline adjuvants. All the animals in this series were passively sensitized with rabbit anti-egg-albumin serum. When tested with egg-albumin, twenty-one of twenty-two untreated animals and six of eight treated with saline and adjuvants died in anaphylactic shock in five minutes. Of the fourteen animals treated with alum-precipitated histamine azoprotein, only one died. All the animals treated with histamine azoprotein and adjuvants or human serum with adjuvants survived. Four guinea pigs were injected subcutaneously with the alum-precipitated preparation. When these animals were tested intravenously with histamine azoprotein solution three weeks later, three died. Hence, although histamine azoprotein confers little or no protection against histamine shock in guinea pigs, it does protect them against passive anaphylaxis. For this purpose immunization with human serum with adjuvants appears as effective as histamine azoprotein. Guinea pigs may be sensitized with one or two subcutaneous injections of azoprotein. E. WALZER.

The Behavior of Platelets in Anaphylactic and Peptone Shock. Fidler, E., and Waters, E. T.: J. Immunol. **52**: 315, 1946.

Platelet changes were studied in dogs in anaphylactic shock and peptone shock. Within two to ten minutes after injection of the antigen into sensitized dogs, the platelet level fell to between 2 to 20 per cent of the original count. Clumping involved from 40 to 90 per cent of platelets. Paralleling the recovery from shock, the platelet count gradually returned to normal and approached 50 per cent of the original level in the first hour. Peptone produced a reaction in dogs very similar to anaphylactic shock, with similar effects on the platelet count. The injection of heparin before the shocking dose of antigen did not prevent the fall in the platelet count or the clumping. Low platelet counts similarly occurred when anaphylactic shock was produced in the dehepatized animal. Clotting time was increased during anaphylactic shock in the dehepatized as well as in the intact animal. It is suggested that the increased clotting time is due not to heparin liberation but to the diminution in platelets. Hence, in anaphylaxis in the dog, the platelet count is of value as an index of sensitivity in mild or doubtful cases. J. SHERMAN.

Experimental Production of Anaphylactic Pulmonary Lesions With the Basic Characteristics of Rheumatic Pneumonitis. Gregory, J. E., and Rich, A. R.: Bull. Johns Hopkins Hosp. **78**: 1, 1946.

Fifty-six rabbits were given repeated intravenous injections of sterile horse serum, egg-albumin, or a combination of both. Histologic sections of the lungs revealed, in ten animals, small focal lesions chiefly characterized by alveolar capillary damage with thrombosis and edema. Six of the animals had died within twenty-four hours of their last injection, two of these in acute anaphylactic shock. One other animal died spontaneously. Five of these seven animals were found to have focal hemorrhages in the lungs. Three animals were killed from one to nine days after their last injection. All three of these rabbits had capillary thrombi in the lungs and two had leucocytic infiltration of the alveolar walls with focal intra-alveolar edema. None had focal hemorrhages. These lesions are basically of the type found in the lung in rheumatic fever.
E. KAILIN.

The Immunochemistry of Allergens. VIII. Precipitin Formation and Passive Transfer Reactions With Allergenic Proteins From Cottonseed and Castor Beans. Coulson, E. J., Spies, J. R., Jansen, E. F., and Stevens, H.: J. Immunol. **52**: 259, 1946.

Studies were made in rabbits on the precipitin formation induced by the administration of CS-1A and CB-1A (proteic-polysaccharidic fractions of cottonseed and castor bean, respectively) and crystalline ovalbumin. The capacities of these antisera to induce passive sensitization in guinea pigs was also investigated. Rabbits were actively sensitized and bled at varying intervals. Ovalbumin was found to be a more effective precipitin producer than CS-1A or CB-1A. The concentration of precipitins for the latter antigens was weak after the first course of sensitization, but was increased after resensitization one month later. The minimal passive sensitizing doses in guinea pigs for anti-ovalbumin sera were consistently smaller than those for CS-1A and CB-1A. For the latter antigens, the MSD was always smaller after resensitization. The MSD of antisera for CS-1A and ovalbumin were unchanged after storage of the sera at 6° C. for almost five years. Hence, CS-1A and CB-1A were precipitinogenic when administered to rabbits but less uniformly effective than ovalbumin. Passive transfer provided a more sensitive method for detecting antibodies than the precipitin method but there was a rough parallelism between the two techniques. E. WALZER.

Modification of Anaphylaxis by Benadryl. Wells, J. A., Morris, H. C., and Dragstedt, C. A.: Proc. Soc. Exper. Biol. & Med. **61**: 104, 1946.

In dogs sensitized to horse serum the intravenous injection of 10 mg. per kilogram of Benadryl prior to the administration of the shocking dose, reduced the severity of anaphylactic shock. There were no deaths in twenty-two animals treated with Benadryl as compared to nine deaths in twenty-six untreated controls. The degree of shock was determined by measuring the carotid blood pressure in the anesthetized animals. Benadryl reduced but did not obliterate the vasodepression of anaphylactic shock. Since previous experience has shown that maximally effective doses do not completely abolish the reaction to histamine in the dog, Benadryl should not be expected to abolish anaphylaxis completely. Benadryl does not interfere with the release of histamine in anaphylactic shock in the dog, but acts antagonistically to it. J. SHERMAN.

Precipitin-Production in Chickens. II. Studies on the In Vitro Rise of the Interfacial Titers and the Formation of Precipitins. Wolfe, H. R., and Dilks, E.: J. Immunol. **52**: 331, 1946.

The precipitin titers of antimammalian chicken sera were studied. It was noted that serum ten or more days old showed a higher titer than serum twenty-four hours old. A rise in titer was found as early as eleven hours after bleeding, with maximal titers between the third and fourth days. A significant rise rarely after bleeding. These high titers were present when tested six months later, occurred after the eighth day and no antiserum showed a rise fourteen days the sera having been frozen or kept sterile in a cold room during this period. Titers were not studied on sera stored for longer periods of time.

The rate of production of precipitins was more rapid after multiple injections than after a single injection. In the former instance, a serum of high titer occurred within three to six days after the last injection, and in the latter instance within five to eight days. Irrespective of the number of injections of antigen, the rise in titer was about the same. The circulating antibodies decreased in two to five hours after injection of the homologous antigen.

J. SHERMAN.

Miscellaneous

The Anti-Histamine Properties of Benadryl, β-Di-Methylaminoethyl Benzhydryl Ether Hydrochloride. Loew, E. R., Macmillan, R., and Kaiser, M. E.: J. Pharmacol. & Exper. Therap. **86**: 289, 1946.

Isolated strips of guinea pig ileum were contracted by small amounts of histamine, barium, or acetylcholine. The histamine contractions were counteracted by Benadryl in dilutions of 1:25,000,000 to 1:50,000,000; the barium contractions by dilutions of 1:66,700 to 1:125,000; and the acetylcholine counteracted by dilutions of 1:2,500,000 to 1:4,000,000. Benadryl was several times more effective in antagonizing barium-induced contractions than was either atropine or papaverine and was half as effective as Trasentin in this respect. In view of these findings, Benadryl cannot be regarded as a specific histamine antagonist. A small series of experiments on dog pressor responses indicated that the depressor response to acetylcholine can be about as effectively counteracted by Benadryl as the depressor response to histamine. After a 3 mg. per kilogram dose of Benadryl the pressor response to ephinephrine was augmented. Atropine in a dose of 0.03 mg. per kilogram similarly enhanced the pressor response to epinephrine. E. KAILIN.

The Preparation and Demonstration of an Antiserum for Trichinella Spiralis. Dorin, R. P.: J. Parasitol. **32**: 83, 1946.

Three rabbits actively immunized with Trichina larvae and five normal animals were fed 20,000 live Trichina larvae orally. Two of the control animals died on the tenth and fourteenth days. One immunized animal was bitten by a cage mate and died on the thirty-second day. On the forty-third day, the remaining animals were killed and various muscles were studied for the presence of Trichina larvae. The two immunized animals with serum titers of 1:5,000 and 1:6,000, respectively, had almost no infestation. The three controls were heavily infested and the serum from these animals showed no immune antibodies for Trichina. Three rats were given intraperitoneal injections of Trichina-immune rabbit serum one day before and one day after the oral administration of 4,500 live Trichina larvae. Three control rats received normal rabbit serum. Eleven days later, the antiserum-protected animals appeared normal and the control rats were moribund. E. KAILIN.

The Duration of Antibody-Formation After Injection of Killed Typhoid Bacillus in Water-in-Oil Emulsion. Freund, J., and Bonanto, M. V.: J. Immunol. **52**: 231, 1946.

The antibody formation of rabbits injected with killed typhoid bacilli in saline was compared with that obtained when the bacilli were combined with adjuvants. Two simultaneous subcutaneous injections of 0.25 ml. typhoid vaccine, either in saline or combined with aquaphor and paraffin, with or without tubercle bacilli, were given to rabbits and repeated after six weeks. Forty-one months later, agglutinin titers ranging from 1:160 to 1:640 were found when adjuvants exclusive of tubercle bacilli had been used. Titers fell below ten in less than a year when vaccine in saline had been injected. Rabbits injected with vaccine and adjuvants, including tubercle bacilli, showed a titer of from 1:320 to 1:640 twenty to thirty-one months later. In a second experiment, rabbits received only two simultaneous injections of typhoid bacilli, with Falba, paraffin oil and peanut oil as adjuvants. Thirty-seven months later, agglutinin titers ranging from 20 to 640 were found. It is inferred that, although the titers were relatively low, antibody formation was proceeding actively during the period of observation. The long duration of the antibody formation emphasizes the lack of relationship between the amount of antigen required and the amount of antibodies formed. E. WALZER.

Allergy Abstracts

Asthma and Hay Fever

Pollen Antigens. Critical Review of Literature. Wodehouse, R. P., and Coca, A. F.: Ann. Allergy **4**: 58, 1946.

The authors have analyzed the "dependable information concerning the biochemical nature of the pollen atopen" and have summarized their conclusions as follows:

"1. Its molecular size is great enough to make it nondialyzable through the usual semipermeable membranes, yet so small as to deny a protein character and to indicate that it is a large-sized complex polypeptide.

"2. Like the higher members of the polypeptides it:

(a) is resistant to heat; not heat coagulable
(b) exhibits a positive biuret reaction
(c) is not easily digestible.

"3. It is an antigen, though a relatively weak one in lower animals.

"4. It appears to be completely a family characteristic among the grasses, though possibly dilute in some species. It appears to be common to the tall and short ragweeds and most likely to all other members of the ragweed tribe; it undoubtedly extends beyond, even to the wormwood group. But further study is needed on this point and to show the extent of its distribution throughout the remainder of the Composite family.

"In all six species of the Chenopod-Amaranth group which have been studied, there is found a common antigen. Among the trees the antigen appears to be never less than a generic character, extending sometimes through related genera and even whole families." AUTHORS SUMMARY.

Pulmonary Acariasis: Its Relationship to the Eosinophil Lung and Löffler's Syndrome. Van der Sar, A.: Am. Rev. Tubere. **53**: 440, 1946.

"Asthmatic bronchitis" was the chief complaint in four of eight patients with chest symptoms hospitalized in the Netherlands West Indies. The remaining four patients did not wheeze but complained of persistent cough. Mites were found in the sputa of all of these persons. Repeated stool examinations for ova and parasites and nightly blood examinations for microfilariae were all negative. The admission blood counts showed an eosinophilia of 58 to 80 per cent in the patients with asthmatoid symptoms and of 14 to 18 per cent in three of the four patients who were not wheezing. The fourth patient showed only 1 per cent eosinophils on admission. In five patients, roentgenologic studies revealed pulmonary infiltrations which were considered characteristic of "eosinophil lung." Transient, ill-defined pulmonary shadows led to the diagnosis of "Löffler's syndrome" in two cases. There was no roentgenologic evidence of any lesion in one patient. Mafarside or Carbason therapy resulted in good clinical response and clearing of the pulmonary lesions. There were no recurrences. E. KAILIN.

Dyspnoea and Diminished Vital Capacity as a Symptom and a Sign in Hay Fever. Brown, E. A., Nobile, C., Sannella, T., and Wadsworth, G. P.: Dis. of Chest **12**: 205, 1946.

Of thirty-eight pollen-sensitive patients subjected to repeated vital capacity determinations, all but twelve showed a diminished vital capacity during the pollen season. Although some of the patients had asthma as a complication of their hay fever, all were free of asthma at the time the vital capacity measurements were made. The possibility that the diminished vital capacity might represent latent bronchial asthma is discussed. In about 30 per cent of the cases, the vital capacity was found to undergo periods of reduction in the absence of any nasal or chest symptoms. In thirty patients, upper respiratory infections were associated with a significant drop in vital capacity.

E. KAILIN.

Production of Aerosols From Medicated Solutions. A Combined Steam Generator and Aerosolizer. Prigal, S. J.: J. A. M. A. **131**: 398, 1946.

A new type of apparatus for aerosolizing medicated solutions is described. Among its advantages are its inexpensiveness, simplicity, and safety. It delivers a warm, moist aerosol which may include more than one medication. Substances, such as propylene glycol, may be used as the diluent in this apparatus. F.

A Case of Tropical Eosinophilia (Weingarten's Syndrome). Hunter, E. A.: Brit. M. J. **1**: 877, 1946.

A 37-year-old European male who had spent twelve years in Nigeria began to have attacks of nocturnal asthma about six months after returning to England. He had had malaria while in the tropics. The white blood count was 12,400, with 59 per cent eosinophiles. X-ray of the chest was negative. A period of freedom from attacks was followed by a recurrence of the malaria and asthma. Another blood count showed 36,200 white blood cells of which 74 per cent were eosinophiles. Three injections of Novarsenobillon given at weekly intervals produced rapid improvement of the symptoms and a normal blood count. F.

Expectorant Action of Volatile Oil. Boyd, E. N., and Pearson, G. L.: Am. J. M. Sc. **211**: 602, 1946.

The expectorant action of the volatile oils and related compounds was investigated in animals. The volatile oils of turpentine, pine, anise, lemon, eucalyptus, and the related drugs terpin hydrate and terebrene were administered by stomach tube to guinea pigs lightly anesthetized with urethane. All of these drugs were found to increase the flow of the respiratory tract fluid. Oil of anise was the most effective of the entire group, and oil of turpentine the most effective terebenthinate volatile oil. About 50.0 mg. of oil per kilogram of body weight was found to be the most effective dose. Compound tincture of benzoin had no apparent expectorant action. Oil of eucalyptus was effective in increasing the respiratory tract fluids of other animal species including the dog and cat. No changes in the specific gravity, chloride content, or concentration of the respiratory tract fluid could be detected following the administration of any of the compounds studied. It was shown that the expectorant effect of these compounds results from their action directly on the secretory cells of the respiratory tract and not from a reflex effect from the stomach. F.

Is There Any Advantage in Combining Several Expectorant Drugs in a Compound Cough Mixture? Boyd, E. M., Palmer, B., and Pearson, G.: Canad. M. A. J. **54**: 216, 1946.

The synergistic action of a combination of expectorants in a cough mixture containing theophylline-ethylenediamine, potassium citrate, wine of ipecac, chloroform, and a syrupy vehicle was studied in animals and human beings. The excretion of respiratory tract fluid (R. T. F.) was used as a measurement of the efficacy of the expectorant in animals. In human beings, the relief from coughing in the presence of a respiratory infection was the criterion. In four of the six species of animals employed and in 72 per cent of the patients, the mixture had an expectorant action. The total expectorant value of the cough mixture was equal to a summation of the values of the individual ingredients. No evidence was found that the mixture influenced the chloride content of R. T. F. It was, therefore, concluded that there was no synergistic action in the combination of expectorants used in the cough mixture. In animals in which the gastric nerves were cut, two-thirds of the expectorant action of the mixture was lost. Hence, two-thirds of the expectorant action could be attributed to a reflex action from the stomach. E. WALZER.

Dermatology

Pyribenzamine in the Treatment of Itching Skin Conditions. Baer, R. L., and Sulzberger, M. B.: J. Invest. Dermat. **7**: 147, 1946.

Pyribenzamine was employed in the symptomatic treatment of a group of fifty-six dermatologic cases comprising seventeen cases of urticaria, eleven cases of atopic dermatitis, and twenty-eight cases of pruritus associated with various dermatoses. The drug was administered in doses of 50 to 300 mg. daily for periods of a few days to several months. Pyribenzamine was effective in relieving the itching in 50 per cent of the cases of urticaria. It was practically of no value in the treatment of atopic dermatitis. Among twenty-eight cases of pruritus due to miscellaneous causes, pyribenzamine diminished the itching in thirteen instances. Approximately 25 per cent of the patients treated developed side effects such as sleepiness, nausea, etc. In two cases, the drug had to be discontinued because of severe side reactions. Although no hematopoietic or urinary complications as a result of pyribenzamine therapy were observed, the authors advise that patients using the drug should be kept under close medical control with laboratory studies at regular intervals during the entire period of use. A.

Ocular Dermatitis From Local Penicillin. Report of 2 Cases. Schultz, A.: Arch. Ophth. **35**: 145, 1946.

Two cases of ocular dermatitis due to local instillation of penicillin are described. In one case, the condition appeared eight days following the daily instillation of eyedrops and the application of penicillin ointment (1,500 Oxford units per milliliter). Patch tests with penicillin were negative, but the cutaneous reaction was positive. A provocative test with one drop of penicillin in saline solution (250 units per milliliter) during a symptom-free interval promptly produced the reappearance of symptoms. In the second case, an ocular dermatitis appeared on the fourth day following the daily instillation of penicillin solution (2,000 units per milliliter). Patch and cutaneous tests with penicillin were positive. C.

Chloroamide-Containing Ointments in the Prevention of Poison Ivy Dermatitis. Sulzberger, M. B., Baer, R. L., and Kanof, A.: J. Invest. Dermat. **7**: 145, 1946.

Twelve subjects highly hypersensitive to poison ivy were satisfactorily protected against experimentally induced ivy dermatitis by a prophylactic application of a chloroamide-containing ointment. These ointments were developed by the Chemical Warfare Service of the United States Army, as protective ointments against mustard gas and other vesicant agents of chemical warfare. Chloroamide-containing gas protective ointments are stable and relatively nonirritating and are said to inactivate vesicant agents by oxidation and chlorination. In the present experiments, the protective capacities of two different chloroamide-containing ointments, a blank control vehicle, and a perborate-containing ointment were tested. The results indicated that chloroamide-containing gas protective ointments of the type developed by the Army offer satisfactory protection against poison ivy dermatitis and probably against other skin irritants and sensitizers. A.

Histamine Content of the Skin: Its Variations Under the Influence of Cold, During Tuberculin Allergy and in Certain Dermatoses. Pellerat, M. J., and Murat, M.: Ann. de dermat. et syph. **2**: 76, 1946.

The average histamine content of the skin in twenty-three normal subjects was found to be 20 mg. per kilogram of weight. Variations in different areas of the same skin zones were negligible. Freezing the skin with ethyl chloride in five subjects caused a marked drop in the histamine content of the frozen skin to 3.9 mg. In the same subjects, the histamine content of skin specimens infiltrated with novocain and adrenalin remained at a high level of 16.4 mg. Proof that the local diminution in histamine content resulted from a liberation of histamine into the blood stream was obtained by comparing the histamine content of venous blood draining the given area of skin before and after freezing. The average increase in the blood of seventy-four subjects was from 65 gamma before freezing to 112 gamma after freezing.

Guinea pig skin freed of its histamine content by freezing with ethyl chloride failed to respond with a second degree burn to the local application of heat. Guinea pig skin anesthetized with novocain-adrenalin and then exposed to heat responded with a second degree burn, indicating that anesthesia alone did not play a part in the protective action of the freezing.

The histamine content of the lesions in cases of skin tuberculosis was found to be quite low when compared with healthy portions of skin in the same subjects. Similar studies of various dermatoses (urticaria, eczema, psoriasis, lichen planus) showed that the histamine content of these skin lesions is always less than that of the adjoining healthy skin. C.

Conjunctivitis and Dermatitis Due to "Beach Apple": Report of 13 Cases. Grana, P. C.: Arch. Ophth. **35**: 421, 1946.

Thirteen cases of acute conjunctivitis and dermatitis of the eyelids and face occurred among troops in Panama following the use, for camouflage purposes, of *Hippomane mancinella L.* (Euphorbiacea) commonly known as "manzanillo" and "beach apple." Another group of ten soldiers who had no actual contact with the plants but worked in their vicinity also developed some symptoms. C.

Death From Hair Dye. Gougerot, H., and Sclafer, M.: Ann. de dermat. et syph. **11**: 296, 1945.

The application of a henna hair dye in a 34-year-old female was followed in twenty-four hours by an intense pruritus, a generalized scarlatiniform erythema, purpura, bulla formation, and edema of all mucous membranes. Death occurred on the seventh day. C.

Otorhinology and Ophthalmology

Histamine-like Substance Present in Nasal Secretions of Common Cold and Allergic Rhinitis. Troescher-Elam, E., Ancona, G. R., and Kerr, W. J.: Am. J. Physiol. **144**: 711, 1945.

A method for the extraction of a histamine-like substance from nasal secretions is described. It is based on principles used in extracting histamine from blood for assay on atropinized guinea pig ileum. This substance is present in the nasal secretions in the "common cold" and in allergic rhinitis. There is no striking difference in total histamine activity between secretions of the "common cold" and those of allergic rhinitis. No correlation was apparent between the number of eosinophiles and the amount of histamine present in the nasal secretions. C.

Is the "Khamseen Cold" (Rhinitis During Sirocco) an Allergic Disease? Gutmann, M. I.: Acta. med. orient. **4**: 47, 1945.

The Khamseen season in Jerusalem occurs between October and June. It is characterized by a desert wind, a dry atmosphere, and specific changes in atmospheric electricity. Khamseens end abruptly with the change to a western breeze and a simultaneous increase in the humidity of the air. During these meteorological phenomena, certain individuals suffer from the symptoms of a head cold which are almost identical with those of vasomotor rhinitis. In an attempt to apply the criteria of allergy to this condition, it was found that, although its clinical course is the same as that of allergic rhinitis, the Khamseen cold is not accompanied by either nasal or blood eosinophilia and is not improved by residence in an allergen-free (air-conditioned) room. Skin tests performed with an extract of the residue of air, filtered during the Khamseen season, were positive in individuals sensitive to air-borne allergens but negative in Khamseen patients. It is concluded that Khamseen cold is not an allergic disease. C.

Atopic Cataracts: Report of Four Cases. Cordes, F. C., and Cordero-Moreno, R.: Am. J. Ophth. **29**: 402, 1946.

Four cases of bilateral cataract formation in patients with atopic dermatitis were observed. All four patients gave positive family histories of allergy, had had eczema in childhood, and showed positive skin reactions to either pollens or foods. One of the patients had, in addition to the cataract formation, an allergic conjunctivitis, a retinal detachment in one eye, and edema of the retina in the other eye. Histologically, the "neurodermatitis cataract" consists of a dense, irregular opaque plaque in the pupillary area just beneath the anterior lens capsule. Thirty to fifty per cent of these cataracts are unilateral. The authors believe that, in these instances of atopic cataract, the lens is the atopic shock organ and that any atopic patient, with or without dermatitis, may have lenticular opacities. C.

Allergic Iritis. Bothman, L: Illinois M. J. **89**: 124, 1946.

In six cases of long-standing iritis in which all possible foci of infection had been eliminated, allergic investigation revealed specific sensitivity to molds, pollens, or foods. Removal of the offending allergens and specific desensitization resulted in a complete disappearance of the eye symptoms. The author advises that allergy be given serious consideration as an etiologic factor in iritis.

Periarteritis Nodosa With Involvement of the Choroidal and Retinal Arteries. Goldsmith, J.: Am. J. Ophth. **29**: 435, 1946.

A diagnosis of periarteritis nodosa was made for the first time intra vitam as a result of ophthalmoscopic observations in conjunction with physical findings and clinical course. The patient had received 232 Gm. of sulfonamides over a period of four months. An aneurysmal dilatation of the fusiform type was observed in the fundus of the right eye involving the inferior temporal artery. Only four other cases have previously been reported with histologic evidence of retinal artery pathology. The author stresses the possibility of inducing hyperergic states within the human body by the administration of sulfonamides and sera. C.

Miscellaneous Allergies

Experimental Studies on Allergic Cholecystitis. DeMuro, P., and Ficari, A.: Gastroenterology **6**: 302, 1946.

The authors present an excellent review of the clinical and experimental evidence for allergic cholecystitis. They report their own experiments performed on rabbits. From ten to fifteen days after sensitization with sheep serum, the gall bladder of the rabbit was exposed and the "exciting" dose introduced into the gall bladder. The cystic duct was ligated in one series of animals, and in another series a tiny glass ball was introduced into the gall bladder to prevent absorption through the mucosa. The animals were then killed at intervals of from one to seventy-two hours later and the gall bladders studied histologically. The reaction in the gall bladder could be divided into a degenerative-exudative phase and a proliferative stage. The chief histologic changes included: (1) a modification of the surface epithelium consisting mainly of degenerative and microbiotic lesions of the mucosa; (2) edema of the various layers, especially the perimuscular connective tissue and the subserous coat; (3) diffuse cellular infiltration containing many eosinophiles; (4) degenerative changes in the muscle fibers; (5) pathologic changes in the vessels; and (6) mesenchymal reaction.

The writers believe that these pathologic changes confirm the existence of allergic cholecystitis. H.

The Role of Histamine and Acetylcholine in the Mechanism of Heat Allergy. A Report of Studies on a Soldier. Peters, G. A., and Silverman, J. J.: Arch. Int. Med. **77**: 526, 1946.

An 18-year-old soldier, with a positive family and personal history of bronchial asthma, developed mild shock and urticaria following exercise. Epinephrine gave prompt relief. The patient stated that similar attacks had occurred after exercise during the previous two years. Experimentally, the urticarial reaction could be produced by exercise, exposure to heat, and by the subcutaneous injection of a combination of histamine and Furmethide (chemically related to acetylcholine). The administration of epinephrine and

atropine inhibited the reaction, but ephedrine failed to do so. Histamine when administered alone appeared to have some inhibitory effect. A period of refractoriness, lasting for about five hours, followed an attack of urticaria. There was a definite delay in the patient's sweating response over the general body surface. There appeared to be an inherent defect in the patient's thermoregulatory system which, under proper conditions, caused an excessive release of histamine and acetylcholine resulting in urticaria. Desensitization with both histamine and acetylcholine was proposed as a method of treatment. F.

The Initial Lesions of Periarteritis Nodosa. Nicaud, P.: Presse méd. **6**: 88, 1946.

The early lesions in periarteritis nodosa consist of an inflammatory reaction of the adventitia characterized by a blanket of polymorphonuclear or lymphocytic cells, mixed with histiocytes. The thickness of the adventitia is quite marked, and the inflammatory cells obscure its texture. The media is essentially normal at this stage, but the intima does show evidence of hyperplasia. These lesions which occur in the early stages of the disease are rarely noted, but they may frequently be found in the smaller vessels near typical skin nodules. C.

Periarteritis Nodosa. Clinical Manifestations and Postmortem Findings With a Report of Six Cases. Higgins, W. H.: South. M. J. **39**: 453, 1946.

Six cases of periarteritis nodosa are presented. A detailed description of the clinical and postmortem findings in one case is given. The clinical manifestations and laboratory findings appeared to vary depending on the organs involved and the stage of the disease, although there was a similarity of symptoms in all six cases. Laboratory studies were usually not helpful in the diagnosis unless an eosinophilia was present. A biopsy was usually not diagnostic, since a section of muscle rarely contained the specific vascular changes. The most satisfactory materials for biopsy were vascular nodules or skin lesions, such as purpuric spots. The diagnosis of periarteritis nodosa should be entertained in all patients with obscure generalized symptoms. J. SHERMAN.

DHE45 (Dihydroergotamine) in the Treatment of Allergic Migraine. Clein, N. W.: Ann. Allergy **4**: 128, 1946.

Twenty-eight cases of migraine were treated with subcutaneous injections of dihydroergotamine (DHE45). Twelve cases were of unknown etiology and only three of these were definitely relieved. Sixteen cases had associated allergic symptoms, such as allergic rhinitis, asthma, or urticaria. Eleven of these obtained relief with the drug within one to three hours. No other medication had been successful in relieving these patients. It was noted on these studies that, if the first injection failed to afford relief, subsequent injections were of no value. Toxic symptoms were negligible. All allergic patients in this series were under active allergic management. J. SHERMAN.

Studies on Filariasis. I. Serological Relationships Between Antigenic Extracts of Wuchereria Bancrofti and Dirofilaria Immitis. Warren, V. G., Warren, J., and Hunter, G. W.: Am. J. Hyg. **43**: 164, 1946.

Complement fixation tests were performed on serum taken from a patient with a clinical diagnosis of filariasis, with antigens prepared from *Wuchereria bancrofti* and *Dirofilaria immitis*. The serum did not fix complement in the presence of *W. bancrofti* antigen even though motile microfilaria were present in the serum. Positive complement fixation did occur with *D. immitis* antigen.

Intracutaneous testing with both antigens in thirty-two patients with clinical filariasis revealed that the *W. bancrofti* antigen yielded as reliable results as *D. immitis* antigen. Specific sera could be produced in rabbits by prolonged immunization with microfilarial suspensions. Using such sera with complement fixation and absorption techniques, the authors found group-specific and species-specific antigenic factors present in both filarial worms. H.

Atabrine as a Cause of Fatal Exfoliative Dermatitis and Hepatitis. Agress, C. M.: J. A. M. A. **14**: 131, 1946.

Atabrine, although generally believed to produce almost no serious reactions aside from toxic psychosis, was found to be the cause of severe hepatitis and generalized exfoliative dermatitis which proved to be fatal in three of the five cases reported. All five reactions occurred among Chinese soldiers and represented about one reaction in every two to three thousand cases treated with the drug. Clinically, the reactions were all similar, consisting of either a scarlatiniform, maculopapular, or a dry scaling rash followed by desquamation. The onset of the rash occurred as early as the second or as late as the tenth day after as little as 0.1 Gm. of atabrine. All cases had been previously exposed to the drug. In addition to the rash, conjunctivitis and exfoliation of the tongue occurred. Jaundice resulting from hepatitis, together with high septic fever and leukocytosis, usually appeared several days after the appearance of the rash. Eosinophile counts were as high as 45 per cent. The urine contained bile but usually no urobilinogen. The liver which at first was enlarged and tender rapidly shrank in size. Mental disturbances were a constant feature in the five cases reported. The patients ran a gradual downhill course with death in coma in the third to fifth week. The case histories are reported in detail. Four of the five cases gave positive patch tests for atabrine. A study was made to evaluate the patch tests with atabrine. Those tests which were allowed to remain in place for twenty-four hours were found to be the most reliable, giving only 3 per cent false positive reactions in patients with normal skins and 8.3 per cent false positive reactions in patients with dermatitis. Treatment for the reaction should be prompt and should include the use of vitamin C, liver extract, intravenous glucose, and plasma. The immediate withdrawal of the drug is important. F.

Delayed Serum Sickness Reaction to Penicillin. Gordon, E. J.: J. A. M. A. **131**: 727, 1946.

The incidence of urticarial reactions to penicillin is relatively low, perhaps less than 1 per cent. The incidence of the delayed serum sickness type of reaction is even less common, probably less than 0.075 per cent. Three cases of delayed reactions to penicillin were observed. The onset of the reactions occurred from two to seven days following the cessation of therapy. Among the common symptoms were severe malaise, low grade fever, tachycardia, severe urticaria, arthralgia, joint effusions, and exfoliative dermatitis of the hands. The reactions lasted from seven to ten days and were not influenced by any form of therapy except epinephrine which afforded only temporary relief. F.

Thioglycolic Acid Poisoning in Connection With the "Cold Wave" Process. Cotter, L. H.: J. A. M. A. **131**: 592, 1946.

Thioglycolic acid is the active ingredient of a "cold wave" process which has been the cause of a large number of toxic and allergic reactions. Among the symptoms are rash, edema, pruritus, nervousness, dizziness, headache,

weakness, dyspnea, and gastrointestinal disturbances. Abnormal findings include, granulocytopenia, elevation of the alkaline phosphatase, changes in the free cholesterol-cholesterolester ratio, and a positive cephalin flocculation test. Five representative cases are reported. The reactions occurred after single or multiple applications. Allergic reactions following a primary exposure are explained by the fact that such persons developed a group sensitivity through previous use of certain depilatories containing the HS radical. The effect of thioglycolic acid is cumulative, and remissions occur after all contact has ceased. Allergic and anemic individuals are said to be most susceptible. F.

Treatment of Headache With Intravenous Sodium Nicotinate. Goldzieher, J. W., and Popkin, G. L.: J. A. M. A. **131**: 103, 1946.

Various types of headaches including migraine were treated by the intravenous administration of 100 mg. of nicotinic acid or its sodium salt equivalent. Of 100 cases treated, seventy-five obtained complete relief. Postspinal-tap cephalgia, migraine, and severe idiopathic headache responded dramatically to this form of therapy. Relief from symptoms appeared to be directly related to the degree of peripheral flush which came on shortly after the beginning of the injection. F.

Allergic Reaction to Parenteral Penicillin. Haswell, R. E., and Wilkinson, J. F.: Lancet **1**: 308, 1946.

Of fifty-six cases with severe and resistant cutaneous infections, which were treated with sodium penicillin parenterally, four developed allergic reactions resembling serum sickness within six to twelve days after the first injection. In all cases, local penicillin treatment had been employed previously. Patch, scratch, and intracutaneous tests were negative in all cases. Symptoms consisted of malaise, urticaria, fever, transient angioneurotic edema, slight general adenopathy, and, in one case, effusion into the shoulder joint. H.

Anaphylaxis

Studies on the Physiology of Anaphylactic Shock. I. Anaphylactic Shock in the White Rat; Experiments in Vivo. Hochwald, A., and Rackemann, F. M.: J. Immunol. **53**: 191, 1946.

Anaphylactic shock is difficult to produce in rats. The rat is a poor precipitin producer; precipitins appear early but are scant and disappear quickly. The rat is susceptible to shock only between the tenth and fifteenth day after sensitization. The symptoms are mild and only half of the animals show symptoms, with no fatalities resulting. Sensitization depends less on the size of the dose or the number of sensitizing doses than on the length of incubation period. Thiamin (vitamin B_1) deficiency failed to influence the anaphylactic reaction. Ascorbic acid administered during the sensitization period increased the severity of anaphylactic shock. This was attributed to the increased antibody titre produced by ascorbic acid. Thyroxin, given shortly before the shocking dose, also increased the severity of shock. Ascorbic acid, given during sensitization followed by thyroxin given before the shocking dose, caused the most severe anaphylactic reactions. J. SHERMAN.

Histamine Antagonists. V. Comparison of Benadryl and Pyribenzamine in Histamine and Anaphylactic Shock. Friedlaender, S., Feinberg, S. M., and Feinberg, A. R.: Proc. Soc. Exper. Biol. & Med. **65**: 65, 1946.

The relative values of Benadryl and Pyribenzamine in protecting guinea pigs against histamine and anaphylactic shock were investigated. For all

unprotected animals, 0.4 mg. per kilogram histamine was found to be the lethal dose. When 3 mg. per kilogram of Benadryl was administered intraperitoneally fifteen minutes prior to the injection of histamine, five times the lethal dose of histamine was required to cause death. When 3 mg. per kilogram of Pyribenzamine was given, 15 mg. per kilogram histamine (37 L.D.) was needed to produce fatal shock. Guinea pigs which were passively sensitized by the subcutaneous injection of 0.5 c.c. rabbit antihorse serum were protected by 1, 2, or 3 mg. per kilogram of Benadryl or Pyribenzamine administered intravenously prior to a shocking dose of horse serum. In all animals tested, 1 or 2 mg. per kilogram of either drug offered significant protection, and 3 mg. per kilogram protected against fatal anaphylaxis. Pyribenzamine on a weight basis offered greater protection against histamine shock than did Benadryl. No difference was discernible between the two drugs in preventing anaphylaxis in passively sensitized guinea pigs. E. WALZER.

The Antigenic Properties of Fibrin Films and Foams Prepared From Human and From Bovine Blood Plasma. Glynn, J. H., and Richardson, J. H.: J. Immunol. **53**: 143, 1946.

Human and bovine fibrin film and foam are strongly antigenic in rabbits when implanted either intraperitoneally or subcutaneously but are not antigenic after heat sterilization. Heated fibrin foam or film is antigenic only when introduced intraperitoneally in finely divided suspension. Even in this form the antigen produces only a small amount of antibodies which react only with unheated antigen. There is, therefore, little contraindication to the surgical use of human fibrin film and foam or of the heated fibrin film and foam derived from a foreign species of plasma. J. SHERMAN.

Transitory Pulmonary Infiltrations (Löffler's Syndrome) in Rabbits. Herbut, P. A., and Kinsey, F. R.: Arch. Path. **41**: 489, 1946.

Experiments designed to produce "allergic pneumonia" in rabbits are described. Horse serum was administered intratracheally to sensitized rabbits. Within a few minutes cough, sneezing, and inspiratory dyspnea were noted. Recovery was rapid. A few râles could be heard in all animals. These respiratory symptoms became worse with each successive intratracheal instillation. Anaphylactic death occurred in only one animal. Little change in rectal temperature was recorded. There was a very slight increase in the white blood count of the reacting animals. X-ray studies of the lungs revealed transitory pulmonary infiltrations, not uniform in distribution, which cleared in from seven to thirteen days. These pulmonary shadows were not migratory in character. Pathologic studies showed congestion, edema, and eosinophilic infiltration of the trachea and bronchi. The lung parenchyma was characterized by congestion, edema, atelectasis, emphysema, and eosinophilic pneumonia. H.

Miscellaneous

The Influence of Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl) Upon Normal Persons and Upon Those Suffering From Disturbances of the Autonomic Nervous System. Preliminary Report. McGavack, T. H., Elias, H., and Boyd, L. J.: J. Lab. & Clin. Med. **31**: 560, 1946.

A majority of the subjects studied became more placid and slept better while receiving Benadryl. Fatigue and sleepiness were noted in 15 per cent of thirty-six individuals. Oral therapy failed to alter the pupil size of nine persons, but the topical application of 0.5 to 1.0 per cent Benadryl produced

mydriasis and interfered with accommodation. Epinephrine, 1 per cent, applied locally with the Benadryl hastened the onset but did not intensify the mydriasis.

Dizziness and blurred vision occurred in two patients with "gastrointestinal neurosis" and in one with dysmenorrhea but were not noted in normal individuals. Three of forty-six patients showed an average depression of blood pressure of 15 mm. Hg. Six patients developed orthostatic hypotension. Benadryl did not seem to exert a greater depressor effect in individuals with disturbances of the autonomic nervous system than in normal individuals. Oral Benadryl medication markedly decreased the response of the skin to histamine injected intracutaneously. However, "for a brief period after the drug was discontinued, the response to histamine was increased." The capillary permeability of six subjects was moderately decreased by the administration of 300 to 400 mg. of Benadryl per day for three to four weeks.

Gastric acidity curves showed a marked decrease in both total and free acid and a diminished response to histamine after Benadryl had been administered for from two to four weeks.

A favorable therapeutic effect was reported in patients suffering from certain "gastrointestinal neurosis," asthma (four cases), functional dysmenorrhea, and one case of "local allergy to insulin."

Benadryl administered orally for periods up to eighteen weeks failed to affect the heart, liver, kidneys, mouth-anus food passage time, basal metabolism, or the appearance of the capillary loops of the fingernail bed. Of ten subjects given from 20 to 30 mg. Benadryl intravenously, three experienced transient untoward effects such as chills, dizziness, headache, low back pain, nausea, drowsiness and extreme pallor. E. KAILIN.

The Influence of Benadryl (Dimethylaminoethyl Benzhydryl Ether Hydrochloride) on Gastric Acidity. McGavack, T. H., Elias, H., and Boyd, L. J.: Gastroenterology **6**: 439, 1946.

Benadryl, in doses of from 200 to 400 mg. daily, was administered to eight normal subjects and to five patients with gastrointestinal neurosis for periods of from two to seven weeks. All patients had shown initial values for free and total acid which were within normal range. Following Benadryl a depressant effect on gastric acidity was observed. In one patient, there was a complete absence of free and total acid which was maintained for three weeks. The acid values returned to previous levels at variable intervals after the drug was stopped. This interval varied directly with the dose and length of time the drug was administered. After the administration of 400 mg. daily for seven weeks, the acid values returned to previous levels in three weeks. Gastrointestinal symptoms were not manifested by the group. H.

The Effect of Two New Histamine Antagonists (Benadryl and Compound 63) on Histamine Stimulated Gastric Secretion in the Dog. Sangster, W., Grossman, M. I., and Ivy, A. C.: Gastroenterology **6**: 436, 1946.

These synthetic histamine antagonists were administered in doses of 50 mg. per kilogram subcutaneously to dogs with pouches of the entire stomach and with gastroduodenostomies. No significant reduction of the response of the gastric glands to stimulation by histamine, administered subcutaneously every ten minutes, was noted. Benadryl probably has less affinity for the gastric gland cells than for other cells activated by histamine. H.

The Relationship of the Protein-Reserves to Antibody-Production. II. The Influence of Protein Repletion Upon the Production of Antibody in Hypoproteinemic Adult White Rats. Wissler, R. W., Woolridge, R. L., Steffee, C. H., Jr., and Cannon, P. R.: J. Immunol. **52**: 267, 1946.

Hypoproteinemic rats were put on protein-rich diets and actively sensitized with washed sheep cells. Their hemolysin titres were measured at varying periods following injection. Titres of hypoproteinemic rats which were repleted for eight days with lactalbumin were eight times those of protein-depleted animals. Normal animals had titres twenty-five to thirty times those of hypoproteinemic rats. Titres of animals repleted for two days with dehydrated beef had already begun to show titres higher than those of depleted animals but not so high as those of well-nourished rats. When repletion proceeded for one week, ability to manufacture hemolysins was consistently greater than in depleted animals and, except for the first few days, less than in normals. The relatively high titres for the first few days after a week of repletion was attributed to an excessive rate of protein anabolism at this time. Five milligrams per day of ascorbic acid fed to protein-deficient rats produced no appreciable change in titre levels. Amigen in repletion was found to produce results similar to those obtained with beef. The antibody-producing mechanism of rats was not permanently damaged even after feeding the animals a low protein diet for 191 days. E. WALZER.

Chemical Factors and Their Role in Inflammation. Menkin, V.: Arch. Path. **41**: 376, 1946.

The inflammatory reaction follows a fundamental pattern in its development. This pattern is conditioned by various factors that can be extracted from the exudative material of the inflammatory reaction. Leukotoxine, one of these factors, is responsible for the increase of capillary permeability and the migration of polymorphonuclear leucocytes. Leukotoxine is probably a product of the injured cells, which also produce glucose. Leucocytosis is caused by a protein in the pseudoglobulin fraction of the exudate, which initiates the discharge of immature granulocytes from the bone marrow and hyperplasia of the megakaryocytes. The canine leucocytosis-promoting factor (L.P.F.) is active and innocuous when injected into man and can produce a rise of from 80 to 150 per cent in the white blood count. Necrosin, a toxic euglobulin factor produced by injured cells, may cause liver and kidney damage. Pyrexin, a glycopeptide, is the factor probably responsible for the fever in inflammation. It acts on the heat-regulating centers of the central nervous system. Purified necrosin is nonpyrogenic. A leucopenic factor has been found to be in close association with pyrexin. Through its action, the white blood cells are trapped in the alveolar walls of the lung and the sinusoids of the spleen. H.

Suppression of Circulating Antibodies in Pyridoxin Deficiency. Stoerk, H. C., and Eisen, H. N.: Proc. Soc. Exper. Biol. & Med. **62**: 88, 1946.

The antisheep hemoglutinin and hemolysin titres of pyridoxin-deficient rats were compared with those of normal animals and those whose growth had been retarded by a restricted full diet. All the rats were injected with three intraperitoneal injections of 0.5 ml. of 5 per cent suspension of washed sheep cells during the fifth week of the dietary regime. Two-thirds of the pyridoxin deficient animals showed no measurable agglutinins or hemolysins, while thirteen of sixteen animals in the control groups had comparatively high titres. Lymphoid hypoplasia was observed in the thymus and lymph nodes of animals deficient in pyridoxin. J. SHERMAN.

Allergy Abstracts

Asthma and Hay Fever

Ethylene Disulphonate. Report of the Council on Pharmacy and Chemistry. J. A. M. A. **131**: 1495, 1946.

The facts about ethylene disulphonate are presented in this report by the Council. Examination of the product indicates that by ordinary tests, both physical and clinical, it is indistinguishable from distilled water. The claim that it contains so-called "ethylene disulphonate" in concentrations of 1:10-15 could not be substantiated. The formula of ethylene disulphonate is one with which chemists are totally unfamiliar. The report states that the product is without therapeutic value and finds it unacceptable for *New and Nonofficial Remedies.* F.

Mites (Acarina) Probable Factor in Etiology of Spasmodic Bronchitis and Asthma Associated with High Eosinophilia. Carter, H. F., and D'Abrera, V. St. E.: Tr. Roy. Soc. Trop. Med. & Hyg. **39**: 373, 1946.

Various species of mites were found in the lungs or urine of 25 Ceylonese patients who had been suffering from respiratory disorders for periods varying from three weeks to seven years. Symptoms disappeared after treatment with organic arsenicals, and the eosinophilia dropped considerably from 3,000 per cubic millimeter. The types of mites found in the sputum were essentially those commonly associated with stored products, dust, and debris. The authors believe that the mites are inhaled, and breed in the lungs or bronchi. Infestation with mites may be of long duration and the conditions known as "pseudotuberculosis," "eosinophile lung" and "tropical eosinophilia" may be explained, in part, on the basis of mite infestation of the respiratory system. C.

Combined Penicillin and Hydrogen Peroxide Aerosol Therapy in Lung Infections. Preliminary Report. Abramson, H. A.: Ann. Allergy **4**: 199, 1946.

A preliminary report is presented on the use of hydrogen peroxide aerosol in cases of asthma, asthma complicated by bronchitis, and bronchiectasis. It was used alone and also alternated with penicillin aerosol. Hydrogen peroxide is readily nebulizable without loss of stability. It is not toxic to mice or to human beings even after prolonged administration. The alternate use of hydrogen peroxide and penicillin aerosol is being tried to combat both Gram-positive and Gram-negative organisms. Results are not yet available. In an addendum, the author describes the results obtained in two advanced adult cases of pulmonary tuberculosis at the end of one month of combined aerosol treatment. In both cases, the cough diminished in severity. Although the sputum remained positive for tubercle bacilli, the Gram-positive organisms disappeared. J. SHERMAN.

Hycodan (Dihydrocodeinone). Stein, P., and Lowy, P.: Am. Rev. Tuberc. **53**: 345, 1946.

The literature is critically reviewed in the light of the authors' three years' experience with hycodan. It is agreed that respiratory depression resulting

from the use of this drug is at least as great as that from morphine, but it has less nauseating and constipating effects. Since bronchospasm is not relieved, the use of this drug in asthmatic patients is considered "dubious." In nine patients who were studied intensively, both codeine and hycodan decreased sputum output. In six of these patients cough was better controlled with hycodan.

Dermatology

The Biological Assay of Poison Ivy Extract. Dunn, J. E., and Smith, B. S.: J. Invest. Dermat. **7**: 185, 1946.

The allergenic potencies of poison ivy extract, poison oak extract, hydrourushiol, and anacardol were assayed in guinea pigs and human beings and their cross-sensitivities studied. The minimal reacting dose (M. R. D.) of each substance was used as an end point and cross-sensitivity was expressed as a ratio of M. R. D.'s. All of 10 human subjects who were clinically sensitive to poison ivy reacted positively to hydrourushiol. Six of these subjects were tested with all four materials. Anacardol failed to give cross reactions in two subjects. In general, poison ivy was the most potent of the substances tested, hydrourushiol the least, and anacardol and poison oak were intermediate. The P. I./P. O. ratios in two cases were 2.7 and 8.2 respectively. Guinea pigs were sensitized to each of the substances and retested with all of them. Poison ivy extract was four times as potent as poison oak extract in animals sensitized to poison ivy. In hydrourushiol-sensitive animals, the poison ivy extract had an assay ratio of 2.56, and poison oak of 11.5, based on the logarithmic mean of the observed ratios. In animals sensitized to poison oak, poison ivy extract remained more potent than poison oak extract. Anacardol proved to be a poor sensitizing agent. It was concluded that poison ivy extract was 4.5 times as potent as poison oak extract. "Comparison of these extracts on human beings was of the same order of magnitude." Hydrourushiol was found satisfactory as a standard material against which poison ivy and poison oak extracts might be compared; anacardol was not. E. WALZER.

Evaluation of Beta-Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl) in the Treatment of Urticaria, Scleroderma and Allied Disturbances. O'Leary, P. A., and Farber, E. M.: Proc. Staff Meet., Mayo Clin **21**: 295, 1946.

When 35 patients with acute urticaria were treated with benadryl taken orally in 50 to 100 mg. doses every three or four hours, 20 were completely relieved, 12 were improved, and 3 were unaffected. Benadryl relieved 48 of 75 patients with chronic urticaria, caused some improvement in 17, and was not beneficial in ten. It relieved severe paroxysms of itching in 8 of 25 patients with atopic dermatitis, and afforded relief in only 6 of 38 patients suffering with pruritus from other causes (jaundice, contact dermatitis, psoriasis, etc.). Among 9 patients with acroselerosis and 4 with scleroderma, receiving 200 to 800 mg. of benadryl per day, 7 of the acroselerotic patients experienced temporary reduction of their edema, but the effect was sustained in only two. Of all patients treated with benadryl, 31 per cent experienced side reactions including drowsiness, dizziness, and dryness of the mouth, in that order of frequency. Side reactions occurred late in 10 patients after several months of therapy. Benadryl does not have a cumulative action, is not habit forming, and may be given for many months without deleterious effects. No skin manifestations of cutaneous sensitivity were observed. E. WALZER.

Effect of Pyribenzamine on Dermographism (Urticaria Factitia). Baer, R. L., and Sulzberger, M. B.: J. Invest. Dermat. **7**: 201, 1946.

Studies were made on a subject who responded with marked whealing at sites where adhesive tape was pulled off the skin. A strip of adhesive tape applied to the left upper back of the patient was removed after fifteen minutes. Within five minutes a pronounced linear wheal formed over the site of application. When the reaction had reached its maximum, seventeen minutes later, the subject took 150 mg. of pyribenzamine orally. After thirty-five minutes another adhesive strip was applied to the right side of the back for fifteen minutes and was then pulled off. After five minutes, this test site showed marked erythema and formation of small wheals with some coalescence. The first test site ran its regular course. It was concluded that the administration of pyribenzamine before the application of the stimulus led to a marked reduction, but not complete inhibition of the urticarial response. The drug had no effect on the course or duration of the dermographic wheal induced before its administration. A.

Epidermal Sensitivity to Penicillin. Gottschalk, H. R., and Weiss, R. S.: Arch. Dermat. & Syph. **53**: 365, 1946.

Two hundred volunteers ranging from 16 to 70 years of age were patch tested with a penicillin ointment containing 500 units of penicillin per gram in a water miscible base. The patches were removed forty-eight hours after application, and the reactions were observed at intervals up to 110 hours. Ten days later, the procedure was repeated. Patches with ointment base were used as controls. Patients who reacted to the ointment were patch tested with an isotonic saline solution containing 10,000 units of penicillin sodium per cubic centimeter and also with a 25 per cent acetone extract of *P. notatum*. Of 200 subjects, nine had either received penicillin previously or had had prolonged contact with penicillin salts. Of these, eight showed positive reactions to penicillin ointment, and four were positive to penicillin sodium solution. None gave positive reactions to *P. notatum* extract. Twenty-four of 191 cases, none of whom had had previous contact with penicillin, showed positive reactions to the ointment on the first trial. Of these, eight reacted to the base and eleven to penicillin sodium. None reacted to *P. notatum*. When those who had not reacted to the first trial were retested, seventeen reacted to the ointment; of these, eight reacted to the ointment base. It was assumed that the others had been sensitized to penicillin, although only one had a positive reaction to penicillin sodium or *P. notatum*. Hence, penicillin used locally was capable of producing contact reactions in 4.5 per cent of the 200 subjects, but it was not a primary irritant in the concentrations used. E. WALZER.

Dermatitis Resulting from Exposure to DDT. A Preliminary Report. Stryker, G. V., and Godfroy, B.: J. Missouri M. A. **43**: 384, 1946.

Six cases of dermatitis resulting from exposure to DDT were studied. Although dermatitis from DDT has been previously reported in the literature, the causative factor has always been shown to be the solvent used as a base. In the present series of cases, all the individuals except one were employed in the manufacture of DDT. The sixth individual had had two exposures to DDT in solution. The skin lesions observed consisted of tiny erythematous areas, either discrete or in clusters. Many of the macular lesions were purpuric. All six patients showed identical lesions. The onset always occurred in the summertime during periods of heavy perspiration. The lesions began on the ankles and extended slowly up the legs and onto the trunk and upper extremities. The face was never involved. The dermatitis was most marked in the skin folds and at

pressure points. The clinical course was protracted, and thereby consisted of the intravenous administration of ascorbic acid. Laboratory studies were all negative. A biopsy of the skin lesions revealed no changes in the structure above the prickle-cell layer. Edema of the cutis and of the papillary layer with some extravasation of red blood cells was noted. The blood vessels were dilated and surrounded by a layer of lymphocytes. It is concluded that the eruption is in the nature of a dermatitis medicamentosa rather than of a dermatitis venenata. The offending agent is either absorbed through the skin or inhaled, and is carried by the blood stream to various skin areas. Patch tests were not performed, since the clinical findings suggested a toxic dermatitis rather than a contact dermatitis. Three patients who returned during the winter months to their previous occupation in the manufacture of DDT experienced no recurrence of symptoms, which suggests that absorption through the skin is the chief portal of entry. A.

Generalized Angioneurotic Edema Due to Penicillin. Inhalations Treated with Benadryl. Scheinberg, D.: J. A. M. A. **132**: 79, 1946.

A 54-year-old man developed angioneurotic edema, urticaria, and arthralgia during the tenth day of treatment with nebulized penicillin. The entire symptoms complex was promptly controlled by the use of benadryl. F.

Dermographia; Another Side Effect of Penicillin Therapy. Kalz, F.: Arch. Dermat. & Syph. **54**: 66, 1946.

Dermographia was observed in 8 patients who developed generalized pruritus after parenteral penicillin treatment. The dermographia began during or shortly after the cessation of therapy and lasted from two to eleven weeks. Five of the patients gave a personal history of urticaria but none had ever had dermographia. A.

Otorhinology and Ophthalmology

Penicillin Aerosol and Negative Pressure in the Treatment of Sinusitis. Barach, A. L., Gaithwaite, B., Rule, C., Talbot, T. R., Kernen, J., Babcock, J., and Brown, G.: Am. J. Med. **1**: 268, 1946.

An apparatus with which aerosol penicillin under negative pressure was introduced into the paranasal sinuses was employed to treat 47 cases of acute and chronic sinusitis. Some of the cases were complicated by the presence of asthma or nasal allergy. Improvement in symptoms was noted in a large percentage of the patients after treatment periods of from three to fourteen days. Clinical improvement was frequently found to be accompanied by improvement in the x-ray findings. Patients with complicating allergies experienced much less improvement than did those with uncomplicated infectious etiologies. F.

Effect of Zephiran Chloride, Tyrothricin, Penicillin, and Streptomycin on Ciliary Action. Greenwood, G., Pittenger, R. E., Constant, G. A., and Ivy, A. C.: Arch. Otolaryng. **43**: 623, 1946.

Aqueous solutions of zephiran chloride (1:100 and 1:2,000) and aqueous suspensions of tyrothrycin were deteterious to the ciliary activity of the extirpated nasal mucosa of rabbits. Equally harmful was the distilled water used as a control. However, neither zephiran chloride (1:1,000 and 1:2,000) in isotonic solution of sodium chloride nor isotonic solution sodium chloride alone had any appreciable deleterious effect on the ciliary action. No apparent

deleterious effects were noted with penicillin in concentrations up to 500 units per cubic centimeter nor with streptomycin in concentrations up to 1,000 units per cubic centimeter of isotonic solution of sodium chloride. C.

Inflammations of Accessory Nasal Cavities and Penicillin Treatment. Rendi, L.: Schweiz. med. Wchnschr. **76**: 189, 1946.

Good results are reported in the treatment of five cases of chronic pansinusitis with polyposis by the combined use of intramuscular injections and local instillation of penicillin. X-ray follow-up one month later demonstrated the persistence of cure. Penicillin therapy was ineffective in a case of allergic sinusitis and in all cases where bronchiectasis was associated with a chronic suppuration of the nasal accessory sinuses. Penicillin therapy is recommended for acute and chronic inflammation of the accessory sinuses termed "bacterial-allergizing pansinusitis." C.

Miscellaneous Allergies

Allergenic and Anaphylactogenic Properties of Vaccines Prepared from Embryonic Tissues of Developing Chicks. I. Skin Sensitivity Following the Subcutaneous Inoculation of Typhus Vaccines in Man. Plotz, H.: J. Immunol. **53**: 315, 1946.

The allergenic properties of vaccines against yellow fever, typhus, and influenza which are prepared from the embryonic tissue of developing chicks were investigated. Skin tests were performed on 180 normal adults with normal egg yolk and egg white in concentrations of 0.01 mg. N per c.c., and with typhus vaccine in the same concentration. Normal saline was used as a control. The intracutaneous tests were made before inoculation with typhus vaccine, one week after the second subcutaneous dose, and again two to four weeks following the third dose. The three doses of vaccine consisted of 1 ml. each, administered subcutaneously on three successive weeks. Only one subject in the series of 180 individuals tested before vaccination showed positive reactions to typhus vaccine, egg white, and egg yolk, respectively. Positive reactions observed were of the immediate type, occurring within fifteen minutes. The 180 subjects were divided into six equal groups, of which one acted as a control. Each of the five other groups received a different brand of typhus vaccine. In the typhus inoculated groups (150 individuals), four subjects developed skin sensitivity to the whole typhus vaccine alone, four to both egg yolk and egg white, and one to egg yolk, egg white, and typhus vaccine. The single individual who showed skin sensitivity to typhus vaccine, egg white, and egg yolk before vaccination, and those subjects who developed skin sensitivity following vaccination with typhus developed no untoward reactions when subsequently inoculated with typhus vaccine. The author states that, among the many millions of soldiers inoculated with egg-embryo vaccines, severe reactions were rarely encountered except among egg-sensitive individuals. In these cases, the use of washed rickettsial suspensions which are relatively free of egg antigens is recommended. Caution must be exercised in the use of egg vaccines in allergic individuals, especially children. A.

Allergenic and Anaphylactogenic Properties of Vaccines Prepared from Embryonic Tissues of Developing Chicks. II. Anaphylactogenic Properties of Typhus Fever Vaccines and Equine Encephalomyelitic Vaccines. Coulson, E. J., and Stevens, H.: J. Immunol. **53**: 321, 1946.

The sensitizing capacities of typhus and encephalomyelitic vaccines were estimated by determining the minimal dose of vaccine which fatally sensitized

the animal to a shocking dose of the vaccine. Typhus vaccines in doses of 0.004 to 0.008 ml., containing 1.2 to 3.1 mg. of protein nitrogen produced fatal sensitization. Equine encephalomyelitic vaccine produced fatal sensitization in doses of 0.001 ml. and upward. The principal sensitizing agents of both vaccines were identifiable with egg white antigens, and the sensitizing capacities of the vaccine were about one-half that of egg white when computed on a protein-nitrogen basis. Purified rickettsial antigens contain antigens of normal yolk sac but in a lesser concentration than typhus vaccines. The antigenic relationships between various batches of typhus vaccines, normal yolk sac, fresh egg white, etc., were studied by the Schultz-Dale technique. It was found that various types of typhus vaccines were essentially the same in antigenic constitution. Sensitivity induced by yolk-sac-typhus vaccines was due entirely to antigens of normal yolk sac. Yolk-sac vaccines and chick-embryo vaccines contained antigenic constituents which were identifiable with antigens of fresh eggs, and principally with antigens of egg white. About 12 per cent of the protein nitrogen of typhus vaccine, and about 0.4 per cent of the protein nitrogen of equine encephalomyelitic vaccine could be attributed to crystalline ovalbumin. The sensitizing properties of the vaccines could be attributed also to antigens of egg white other than ovalbumin and to antigens of egg yolk. It was concluded from these experiments that immunization with typhus vaccines presents a risk to potentially allergic individuals and a danger to egg-sensitive patients. A.

Allergenic and Anaphylactogenic Properties of Vaccines Prepared from Embryonic Tissues of Developing Chicks: III. A Study to Determine Whether Chick-Embryo Yolk-Sac Vaccines Contain Sufficient Egg Proteins to Cause Severe Systemic Reactions if Given to Egg-Sensitive Individuals. Stull, A.: J. Immunol. **53**: 343, 1946.

Typhus-yolk-sac vaccine-supernate, typhus-yolk-sac vaccine-sediment, normal yolk-sac 10 per cent, pure Rickettsial bodies, typhus-yolk-sac vaccine, equine encephalomyelitic vaccine, egg white, and egg yolk were compared in their reactions with the sera of five egg-sensitive patients, and with serum of one patient in whom egg hypersensitivity had been induced artificially with equine encephalomyelitic vaccine. The passive transfer technique was employed. The relative activity of the egg preparations was determined by a semi-quantitative dilution method. Specificity was determined by quantitative cross-neutralization of egg-sensitive sera. Typhus-yolk-sac vaccine-supernate and whole typhus-yolk-sac vaccine gave positive tests in dilutions approximately ten times that of typhus-yolk-sac vaccine-sediment. Typhus-yolk-sac vaccine-supernate contained at least 10 per cent of the reactivity of egg white, and was slightly more reactive than egg yolk and normal yolk sac. Equine encephalomyelitic vaccine contained egg yolk, yolk sac, and chick embryo, but very little egg white. Pure Rickettsial suspension did not react with egg-sensitive sera. The variability in egg-sensitive sera was apparent in the predominance of sensitivity to egg white in one, to egg yolk and egg white in another, and to yolk sac, yolk, and probably chick embryo in the serum of the patient with induced sensitivity. Hence, the presence of egg white and yolk antigens in egg-embryo vaccines may produce dangerous systemic reactions upon injection in egg-sensitive individuals.

E. WALZER.

Treatment of Allergy to Insulin. Report of One Case. Gastineau, C. F., and Leavitt, M. D.: Proc. Staff Meet. Mayo Clin. **21**: 316, 1946.

A white male, aged 59 years, with a long-standing history of diabetes and recent hemiplegia, was given insulin because of an increasing glycosuria. The

patient had received insulin for two short periods a few years previously without ill effects. After four days of insulin treatment he developed redness, swelling, and pruritus at the sites of injection. During the next ten days of therapy (consisting of 66 units of regular and protamine insulin daily) he developed a generalized urticaria and angioneurotic edema. The oral administration of 250 to 350 mg. of benadryl completely controlled the urticaria, but not the angioneurotic edema. Intracutaneous tests were made with 0.2 c.c. of crystalline zinc insulin before and after the oral administration of benadryl. The flares produced by injections of insulin were reduced after benadryl had been administered. Intracutaneous tests were made also with insulin mixed with a 1:1,000 solution of benadryl. The flares produced by the mixture were smaller than those produced by a similar concentration of insulin without benadryl. Passive transfer studies revealed a high titer of insulin reagins in the patient's serum. When the daily dose of insulin was administered with an equal amount of benadryl solution, local reactions were prevented, but generalized urticaria persisted. A maximum of 98 units of insulin was required to control glycosria at the height of the urticarial reaction, but, as the allergic reaction subsided, the daily insulin requirement dropped to 50 units. A.

The Use of Histamine Antagonist, Beta-Dimethylaminoethyl Ether Hydrochloride, in Allergic Disease. Friedlander, A.: Am. J. Med. Sc. **212**: 185, 1946.

Benadryl was effective in controlling the symptoms of two of 11 cases of chronic urticaria and angioneurotic edema. When the drug was discontinued, symptoms usually recurred. The drug produced no apparent benefit in patients with asthma, hay fever, or allergic headache. Pruritis in atopic eczema appeared to be relieved, but there was no improvement in the skin lesions. Benadryl should not be used over long periods of time without attention to the underlying etiology because of unfavorable side-effects and the increase in tolerance which it produces. F.

Sensitivity to Thiamine Chloride. Engelhardt, H. T., and Baird, V. C.: Ann. Allergy **4**: 291, 1946.

A white woman, aged 42 years with no previous allergic history, had been receiving subcutaneous injections of a vitamin mixture containing thiamine chloride for six weeks. Following a two-month rest period, treatment with thiamine chloride alone was resumed. She was given 100 mg. subcutaneously twice a week. Following the third injection the patient complained of nausea, vomiting, and restlessness. A fourth injection of 50 mg. of thiamine chloride administered about three weeks later resulted in immediate nausea and vomiting. The patient became very weak, and complained of substernal tightness, shortness of breath, and severe generalized pruritus. Urticaria and conjunctivitis were also present. The reaction was controlled by 5 minims of epinephrine. Passive transfer studies were positive with thiamine chloride. The author advises against the use of thiamine chloride parenterally, especially when oral administration serves the same purpose. A.

Folic Acid (L. Casei Factor), an Essential Pan-Hematopoietic Factor: Experimental and Clinical Studies. Doan, C. A., Wilson, H. E., Jr., and Wright, C. S.: Ohio State M. J. **42**: 139, 1946.

Folic acid (L. Casei Factor) has been shown to stimulate hematopoiesis in human macrocytic anemias. L. Casei factor, which was first obtained from liver extract residue, has recently been synthesized. The authors have success-

fully employed folic acid therapy in patients sensitive to liver extract. Three patients with Addisonian pernicious anemia, who had been receiving parenteral liver extract, developed generalized urticaria, local reactions, and anaphylactoid reactions at various times during the course of therapy. Intracutaneous tests made with a 1:10 dilution of liver extract resulted in marked positive reactions. Positive skin reactions were not observed with folic acid. Repeated intravenous injections of folic acid were tolerated without reaction and this form of therapy was successfully employed instead of liver extract. A.

Hypersensitivity in the Pathogenesis of the Histopathologic Changes Associated with Sulfonamide Chemotherapy. French, A. J.: Am. J. Path. **21**: 679, 1946.

Lesions which were apparently attributable to sulfonamide sensitivity in 76 fatalities and skin biopsies from two cases sensitive to these drugs were studied. The total dosage of sulfonamides ranged up to 340 Gm. administered over periods as long as six weeks. The patients were treated for a variety of illnesses, including lobar pneumonia, bronchopneumonia, gonorrhea, fracture, perforated appendix, duodenal ulcer, and otitis media. Clinical complications occurring in one-half the patients and suggesting sensitivity were dermatitis, anuria, icterus, aplastic anemia, fever, chill, blood eosinophilia, hemolytic anemia, and leucopenia, in that order of frequency. In 14 cases, multiple therapeutic courses of sulfonamides were given. The characteristic cell, the acidophilic histiocyte, was found in focal and diffuse infiltrations in the heart, liver, kidney, lung, spleen, lymph node, bone marrow, skin, testis, intestine, gall bladder, prostate, urinary bladder, skeletal muscle, thyroid, aolta, and meninges. Other significant lesions attributed to sulfonamide sensitivity were vascular lesions of fibrinoid necrosis, endothelial edema and proliferation; focal subendocardial, subepicardial, and subpelvic renal hemorrhages; interstitial pneumonitis and hemorrhage into the alveoli. E. WALZER.

Allergy of Joints. Criep, L. H.: J. Bone & Joint Surg. **28**: 276, 1946.

Allergic arthropathies may be divided into five distinct groups: The first group comprises those cases of prolonged chronic infectious arthritis which are regarded by some as a manifestation of bacterial allergy, although there is little evidence to support this supposition. The second group is composed of cases which manifest transient articular swellings as a result of the administration of foreign sera or drugs. In the third group are cases with Henoch's purpura. Although articular swelling does not occur in all cases of Henoch's purpura, a considerable percentage manifests this symptom, which may be due to allergy. In the fourth group are the so-called intermittent hydrarthrosis, characterized by massive recurrent swellings of a joint, usually the knee. The fifth group of cases described by the author is composed of patients who complain of intermittent swellings and pains in the joints which are frequently mistaken for subacute arthritis, except for the fact that there is no evidence of infection. Although the temperature, blood count, and sedimentation rate are usually normal, there may be a mild eosinophilia. These patients usually give a positive personal history of allergy, such as migraine, urticaria, asthma, hay fever, etc. They usually show positive skin reactions to foods, and these sensitivities may be confirmed by clinical trial. Four such cases are described by the author. In each instance, the elimination of the offending foods produced complete relief of symptoms. All of the patients gave a clinical history of food sensitivity and had urticaria or angioneurotic edema. The foods which caused symptoms were tomato, fish, grape, nut, wheat, and egg. The mechanism in allergic arthrop-

athies is the same as that in urticaria and angioneurotic edema, except that the synovial membrane is the shock tissue instead of the skin. There may or may not be exudation into the joint cavities with or without eosinophiles in the fluid.

A.

The Pathology of Sulfonamide Allergy in Man. More, R. H., McMillan, G. C., and Duff, G. L.: Am. J. Path. **21**: 703, 1946.

A review of 375 autopsy records of patients who had received sulfonamide therapy revealed 22 cases in whom lesions attributable to sulfonamides were present. In a control series of 400 consecutive autopsies of patients without sulfonamide therapy, all similar pathologic lesions were explainable on some other etiologic basis. Four of the 22 patients whose lesions could be attributed to sulfonamides had symptoms of painful joints, dermatitis, asthma, and conjunctivitis which were considered allergic and followed administration of the drug. Seven others exhibited severe clinical reactions including: anuria, agranulocytosis, jaundice, fever, and signs of periarteritis nodosa after sulfonamide therapy. Two patients "presented reactions of a suggestive but questionable character." The remaining nine manifested no reactions. It was believed that sulfonamides caused the death of seven patients, was a major factor in the death of another seven, and a negligible factor in eight. Basically, all lesions examined were a complex of tissue destruction and proliferation of the reticulo-endothelial cells in the affected area. These lesions were described as: focal or massive necrosis of the liver and focal necrosis of bone marrow; granulomas of the heart, liver, kidney, lung, bronchus, peritoneum, and fracture callus; interstitial inflammatory lesions of the kidney and liver; polyvascular inflammatory lesions of the arteries of the spleen, liver, kidney, lung, air sinuses, prostate, and renal pelvis; trabeculitis of the spleen; nephrotic lesions; and parenchymatous degenerative changes of the kidney and liver. In all lesions the typical infiltrating cells were large mononuclears and were associated with varying numbers of polymorphonuclears and eosinophiles. These lesions were attributed to sulfonamide therapy because no other common etiologic factor could be found, and because they were similar to many sulfonamide lesions previously reported. Moreover, they were associated with clinical manifestations of sulfonamide hypersensitivity and were similar to lesions produced in animals with foreign protein sensitization.

E. WALZER.

Streptomycin in the Treatment of Infections. Report of 1,000 Cases. Keefer, C. S.: (National Research Council) J. A. M. A. **132**: 70, 1946.

Acute toxic and allergic reactions are frequently encountered in the course of streptomycin therapy. Histamine-like effects such as headache, flushing of the skin, nausea, and vomiting are due to the presence of histamine or histamine-like substances in streptomycin preparations. These symptoms are usually transient. Sensitization reactions, consisting of erythematous, maculopapular, urticarial, or hemorrhagic rashes usually are observed from the third to the tenth day of treatment. However, they may occur as early as the second day or they may appear after treatment has been stopped. Fever may or may not accompany the skin lesions. It is advisable to stop streptomycin therapy if a skin eruption appears, or at least to reduce the dose. Patients who have had rashes frequently react to a single injection of streptomycin with a reappearance of the rash or fever. The longer the time interval between the initial reaction and the reinjection of streptomycin, the less likely is the recurrence of a second reaction. Hypersensitive reactions were observed in four patients between the seventh and eighth days. In one patient, after an interval in treat-

ment of twenty days, an injection of streptomycin produced an elevation in temperature. A second injection the following day produced a skin eruption over previous areas of involvement and an increase in eosinophilia from 2 to 10 per cent. Nine of 11 patients developed eosinophilia of 5 per cent or more, and in eight the eosinophilia persisted as long as the drug was given. In four cases the eosinophilia was associated with a skin eruption. In the other five cases, it began during the second month of streptomycin therapy and was not accompanied by skin lesions. A.

Anaphylaxis

Studies on Ragweed Pollen Sensitization in Rabbits and Guinea Pigs. Kulka, A. M., and Hirsch, D.: J. Immunol. **53**: 391, 1946.

Six rabbits which had received injections of ragweed pollen extracts with or without adjuvants for a year were further studied for a second year. The animals were given higher concentrations of ragweed extract with the same adjuvants, and rest periods of from three to six months were allowed to elapse between injections. Intramuscular injections of 20,000 to 100,000 protein nitrogen units were administered. The antibody-titers of the sera were determined by the collodion-particle method at one- to three-month intervals. Tests for cutaneous sensitivity were made at the same time. The results indicated that repeated injections produce more sensitization and antibody formation than a single injection. Injections are often followed by a temporary fall and then a rise in agglutinins. Once a maximum antibody concentration had been reached in a particular animal, a further rise could not be induced by further injections. Skin sensitivity diminished in spite of the fact that the agglutinative titer was maintained. The ability of the sera to sensitize the skin of normal guinea pigs did not depend upon their titers.

Guinea pigs were injected with ragweed pollen extracts and adjuvants. It was found that the agglutinin titer of the guinea pig sera was directly related to the number of sensitizing injections administered. The sera of 21 out of 24 animals injected with ragweed pollen extracts and adjuvants transferred sensitizing antibodies to normal guinea pig skin. With 16 different guinea pig sera, the human skin was passively sensitized in each instance. There was no apparent relationship between the intensity of the skin reaction produced and the agglutinative titer of the injected sera. In some cases, sera containing no agglutinins successfully sensitized the skin. The degree of skin sensitivity of guinea pigs and their susceptibility to anaphylactic shock could not be correlated with the agglutinative titer of their sera. A.

Pharmacodynamic Studies of a New Antihistamine Agent, N'Benzyl-N-Dimethylenediamine HCl, Pyribenzamine HCl. I. Effects of Salivation, Nictitating Membrane, Lachrymation, Pupil and Blood Pressure. Yonkman, F. R., Chess, D. Mathieson, D., and Hansen, N.: J. Pharm. & Exper. Therap. **87**: 256, 1946.

Experiments were conducted on 35 adult anesthetized cats. Pyribenzamine, in doses of 100 to 200 micrograms administered intra-arterially, failed to affect salivation, retraction of the nictitating membrane, pupillary size, or lachrymation. However, there was a tendency to a sustained rise in blood pressure with larger doses of the drug. The salivary effect produced by 10 micrograms of histamine was inhibited by 5 to 20 micrograms of pyribenzamine or by atropine. When salivation was induced by faradization of the chorda tympani nerve, pyribenzamine not only was devoid of inhibitory effect, but even seemed to enhance the response. Thus, pyribenzamine antagonizes histamine without de-

pressing the tissue directly and without behaving like atropine. Although pyribenzamine antagonized the histamine-induced retraction of the nictitating membrane, the retraction was enhanced in two experiments when epinephrine was used instead of histamine as the eliciting agent. All actions of histamine are not counteracted by pyribenzamine. This drug did not affect histamine-induced mydriasis, and usually failed to counteract histamine hypotension. It is suggested that pyribenzamine may interfere with the destruction of epinephrine in the body. E. KAILIN.

Pyribenzamine (N'-Pyridyl-N'-Benzyl-N-Dimethylethylenediamine HCl), An Antagonist of Histamine. Mayer, R. L., Hays, H. W., Brousseau, D., Mathieson, D., Rennick, B., and Yonkman, F. F.: J. Lab. & Clin. Med. **31**: 749, 1946.

The acute toxicity of intravenous pyribenzamine in mice, rats, and rabbits, expressed as the LD_{50}, was from 9 to 12 mg./kg. When the drug was administered orally, the LD_{50} was 210 mg./kg. for mice, 515 mg./kg. for female rats, and 570 mg./kg. for male rats. Castration of female rats rendered them approximately as susceptible as males. Toxic symptoms consisted of excitement and convulsions, the latter sometimes being superseded by central nervous system depression prior to death. The daily oral administration of 5 mg./kg. doses to white rats for five months produced no apparent ill effects. Fibrosis of muscle tissue was noted after intramuscular injections of the drug. Subcutaneous injections were sometimes followed by skin necrosis. Six human subjects tolerated up to 500 mg. of the drug daily, given in 100 mg. tablets. Mild sedation in one and mild nausea with "pelvic heaviness" in another of these subjects were the only untoward symptoms experienced. Pyribenzamine in amounts of 0.01 to 50.0 micrograms antagonized muscle contractions of guinea pig intestine, uterus, and bronchi induced in vitro by 1.0 mg. of histamine. E. KAILIN.

Studies on the Physiology of Anaphylactic Shock. II. The Reactivity of the Isolated Rat Intestine to Antigen, to Histamine, and to Acetylcholine. Hochwald, A., and Rackemann, F. M.: J. Immunol. **53**: 355, 1946.

In vitro anaphylaxis experiments using the Dale technique were carried out with intestinal strips of rats. Strips of animals sensitized to horse serum all reacted when horse serum was added to the bath. Only 9 of 33 rats could be sensitized to human serum. The best reactions were observed when the muscle strips were tested between the twelfth and seventeenth day after the last sensitizing dose. In most instances, the sensitized muscle responded to the antigen with a contraction. In 8 of 40 muscle strips, the response was a relaxation. Thyroxin and ascorbic acid, when previously fed to the rats, had enhanced anaphylaxis in the whole animal but did not influence the reaction in the bath.

The reaction of the rat intestinal muscle to histamine was not constant, resulting either in contraction or relaxation. In some cases, a 1:1,000 dilution was tolerated without response. The reaction to acetylcholine was uniformly that of contraction. J. SHERMAN.

Significance of Histamine in Trypsin Shock as Determined by Benadryl. Wells, J. A., Morris, H. C., and Dragstedt, C. A.: Proc. Soc. Exper. Biol. & Med. **62**: 209, 1946.

It was shown that benadryl does not protect the guinea pig or the dog against the lethal action of intravenously injected trypsin. Benadryl is less effective in counteracting the blood pressure fall produced by trypsin than that produced by histamine. The low blood histamine levels found in trypsin shock

are not in proportion to the severity of the symptoms. These observations refute the hypothesis that trypsin owes its toxicity to the liberation of histamine from the tissues. J. SHERMAN.

Miscellaneous

The Elimination of Human Reaction-Producing Material from Horse-Derived Antiserums: An Electrical Method. Cardone, C.: J. Lab. & Clin. Med. **31**: 829, 1946.

Pneumococcal and scarlatinal antisera known to be pyrogenic for rabbits and to cause chills, dyspnea, vomiting, or urticaria in man were subjected to the effects of an electric current passed through electrodes which were separated from the antisera by a semipermeable membrane. The sera were then dialyzed for six days against running water. By this treatment the pyrogenic and reaction-producing properties of the sera were considerably diminished. Dialysis without the electric processing or a shortening of the dialysis period reduced the effectiveness of the procedure. The original antibody potency of the materials was retained. E. KAILIN.

Experimental Purpura and Pancreatic Necrosis Produced by Forssman Heterophil Antibody. Grana, A.: Proc. Staff Meet., Mayo Clin. **21**: 298, 1946.

When rabbit anti-sheep serum was injected intravenously into the dog, there was an immediate thrombopenia and leucopenia. After twenty-four hours hemorrhages and purpuric patches of the skin were noted. Intravenous liver glycogen which eliminated nearly all of the blood platelets did not prevent hemorrhages in the lungs when rabbit anti-sheep serum was administered intravenously. Intracutaneous or intraperitoneal injections of serum produced local hemorrhages and edema. When it was given into an artery the organs supplied showed edema, necrosis, and hemorrhagic lesions. Forty-eight hours after the pancreaticoduodenal artery was injected, sections of the pancreas showed necrosis of pancreatic tissue with infiltration of polymorphonuclears, hemorrhage, and edema. It is concluded that this serum produced direct injury to blood vessels. E. WALZER.

Influence of Amino Acid Feeding Upon Antibody Production in Protein Depleted Rats. Wissler, R. W., Woolridge, R. L., and Steffee, C. H.: Proc. Soc. Exper. Biol. & Med. **62**: 199, 1946.

Over a period of six months, protein-depleted rats lost weight and developed low serum protein and hemoglobin readings as compared with normal controls. Addition of amino acids to the diet caused a marked increase in serum protein and hemoglobin concentration, but only a slight gain in weight. Feeding of liver concentrate brought no further response. Antibody response to the intravenous injection of washed sheep erythrocytes was diminished in the protein-depleted rats as compared with normal controls. When the rats were fed amino acids, the hemolysin titer of the blood increased five times over that maintained on a low protein diet. Addition of liver concentrate did not stimulate any further antibody formation. J. SHERMAN.

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